# SURGERY

## GYNECOLOGY AND OBSTETRICS

*An International Magazine, Published Monthly*

VOLUME 75 SEPTEMBER, 1942 NUMBER 3


# DRAINAGE OF THE COMMON HEPATIC DUCT

## With Special Reference to Bile Peritonitis, Wound Infection and Other Complications


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THIS study was undertaken in an attempt to evaluate certain points in the technique of operation on the common bile duct reported by us in 1935 (2). At that time, we described a method of draining the common hepatic duct with a rubber catheter, brought out through a stab wound in the right flank, along with a short cigarette wick, which was placed in the subhepatic fossa (Morison's pouch). We advocated tight closure of the original vertical (right paramedian) incision and stated our belief that this technique would give a lower incidence of infected wounds and incisional hernias. Recently, we published (3) follow-up studies on 775 patients, who had had common duct exploration, with special reference to the graded dilatation of the sphincter of Oddi and reported 4 fatal cases of bile peritonitis. The present analysis includes a review of 18 cases of bile peritonitis in that series of operations.

Of the 775 patients, who had exploration of the common bile duct, there were adequate data for the present study on 744; 479 of these had external drainage of the region established through the main incision, as has been the custom in this hospital for many years. Since there have been an adequate number, 233 cases treated by separate, carefully planned, stab wounds for drainage with tight closure of the main incision, to draw comparisons, we wish to present these data.

Transverse incision was used in only 32 individuals with 3 instances of major wound infection and 3 subsequent hernias in scar. This number is too small to be of much significance and, for this reason, has been excluded from further analysis; the figures, however, suggest an incidence of infection and hernia comparable to that in patients drained through a vertical incision.

Table I shows the types of incision with the number and percentage of major wound infections, wound separations, subdiaphragmatic abscesses, and subsequent hernias in scar.

The table shows that there was at least four times as much major wound infection and eight times as many incisional hernias when drainage was established through the main wound, as when separate wounds were made for drainage. There were 8 cases of complete wound dehiscence following drainage through the main wound, while no such complication


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TABLE I.—TYPES OF INCISIONS AND SEQUELAE

| | Drainage through vertical incision | | Stab wound drainage | | Drainage through transverse incision | |
|---|---|---|---|---|---|---|
| No. cases | 479 | | 233 | | 32 | |
| | No. | Per cent | No. | Per cent | No. | Per cent |
| Major wound infection | 70 | 14.6 | 8 | 3.4 | 3 | 9.3 |
| Dehiscence | 8 | 1.7 | 0 | | 0 | |
| Subdiaphragmatic abscess | 4 | 0.8 | 2 | 0.85 | 0 | |
| Hernia in scar | 34 | 7.1 | 2 | 0.85 | 3 | 9.3 |
| Deaths | 24 | 5.0 | 9 | 3.8 | 0 | |

occurred in any case when drainage was established through a stab incision. There were 4 instances of subdiaphragmatic abscess in individuals drained through the wound and 2 when stab wound drainage was established giving essentially the same percentage. The danger of subdiaphragmatic abscess, as a complication of stab wound drainage, has been stressed as a serious objection to the method. We feel that this important question of drainage has been adequately answered by our experience.

It was found that opening the duodenum increased the incidence of wound infection and this was true whether the duodenum was opened for transduodenal exploration of the common duct or for closure of a fistula between the duodenum and gall bladder.

TABLE II

| | No. of cases transduodenal exploration | No. of cases closure of duodenal fistula | Total cases | Wound infection |
|---|---|---|---|---|
| Stab wound drainage | 8 | 6 | 14 | 4 |
| Wound drainage | 15 | 4 | 19 | 6 |
| Total | 23 | 10 | 33 | 10 |

There were 23 patients in whom the common duct pathological process necessitated transduodenal exploration and 10 who had established a fistula between the gall bladder and the duodenum. In this group of 33 cases, 14 had drainage established through a stab wound. Four of these developed major infection in the primary wound, accounting for one-half of all the cases of wound infection in a total of 233 counter drainage cases. It is fair to state that there have occurred a few cases of minor infection in the stab wound itself. Rarely has this caused serious delay in the convalescence and in no instance did it require further surgery.

TABLE III.—INCIDENCE OF INFECTION EXCLUDING CASES OF OPENED DUODENUM

| | No. cases | No. cases infection | Per cent |
|---|---|---|---|
| Drainage through vertical incision | 460 | 64 | 13.9 |
| Stab wound drainage | 219 | 4 | 1.8 |

During the same period of time, the incidence of sepsis, hernia, and evisceration in wounds drained after operation for acute cholecystitis was practically identical with that of drainage through the wound after common duct exploration (6).

TABLE IV.—INCIDENCE OF SEPSIS, HERNIA AND DEHISCENCE AFTER DRAINAGE

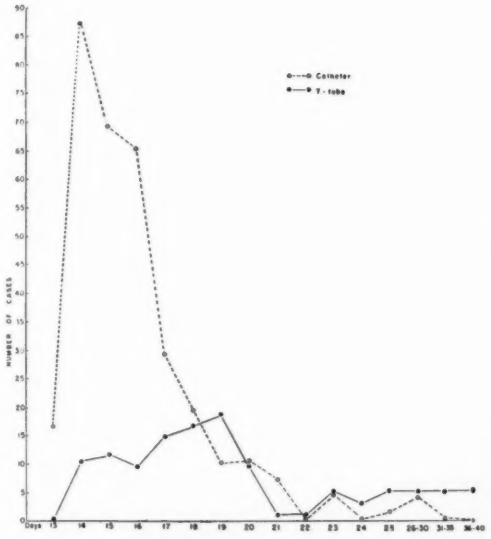
| Drainage through vertical operative incision | Per cent infection | Per cent hernia | Per cent dehiscence |
|---|---|---|---|
| Common duct exploration | 14.6 | 7.1 | 1.7 |
| Operation for acute cholecystitis | 16.6 | 5.5 | 1.5 |

The average postoperative hospital period was 16.1 days following stab wound drainage and 18.7 days following drainage through the wound. Of those patients drained by a stab wound, 75.8 per cent were discharged from the hospital by the 16th day and only 44.7 per cent of those drained through the wound could be discharged that soon after operation. The cause of delayed hospitalization over 20 days for survivors is shown in Table V. Of those with stab wound drainage 9.4 per cent were delayed in contrast to 19.4 per cent whose drainage was established through the operative incision.

TABLE V.—PROLONGED HOSPITALIZATION (OVER 20 DAYS)

| | 233 stab wound | 479 through wound |
|---|---|---|
| Wound infection | 8 | 39 |
| Prolonged bile drainage | 5 | 26 |
| Pulmonary complications | 4 | 7 |
| Bile peritonitis | 0 | 5 |
| Study for other diseases | 1 | 3 |
| Dehiscence | 0 | 4 |
| Subdiaphragmatic abscess | 0 | 2 |
| Miscellaneous | 4 | 7 |
| | 22 | 93 |
| Per cent of total | 9.4 | 19.4 |

The chief reason for prolonged bile drainage was pointed out in previous publications and has no relation to the position of the drainage tube. Greatly prolonged drainage of bile means




Graph 1. Comparative hospital days for patients in whom catheter and T-tube drainage of the common duct is used.

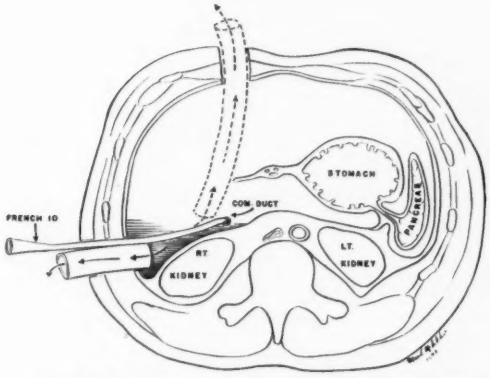



Fig. 1. Schematic drawing, modified after Morison, illustrating cross section of the human body at level of the foramen of Winslow. The shaded area shows the pooling of bile and serous drainage from the gall bladder bed and common bile duct. Note the short cigarette wick draining the region at a low level. The only foreign body left in the area of operation is a small rubber tube draining the common duct in which the opening has been tightly sutured around the tube. This minimizes extravasation of bile elsewhere in the abdominal cavity and adhesions between the duodenum and the gall bladder region. The dotted tube leading through the original incision in the abdominal wall transverses a much longer course and must increase the extent of adhesions, if used.

that adequate outlet for bile into the duodenum had not been established (2, 3).

All cases of bile peritonitis were reviewed and two definite causes were found—closure of the common duct without drainage and failure of the drainage tube to drain bile following operation. All cases with no tube left in the common duct and all cases with no drainage of the bile from the tube used for drainage were analyzed. The similarity of the two groups in regard to bile peritonitis is apparent. The mechanism seems the same in both cases and is essentially bile leakage from the common duct either through the repaired opening or around the nonfunctioning tube; if there is free flow to the outside, the convalescence is smooth, if not, some degree of bile peritonitis occurs, which carried a mortality of 22 per cent.

TABLE VI.—MORTALITY

| | No. cases | Bile peritonitis | Deaths | Per cent mortality with bile peritonitis |
|---|---|---|---|---|
| Common duct closed without drainage | 28 | 9 | 1 | |
| No bile through drainage tube | 29 | 9 | 3 | |
| Total | 57 | 18 | 4 | 22.2 |

There was only 1 case of the 28 closed without a tube in the common duct, which drained no bile into the dressing. This patient had a very large duct and convalescence was quite smooth, which shows that watertight closure can be accomplished; but this is difficult and so generally unreliable that it should, in our opinion, rarely be attempted.

An attempt was made to determine why there was no bile drainage through the tubes used in 29 cases. All of these patients drained bile into the dressing and, as stated previously, those who drained freely to the outside had a

TABLE VII.—NONFUNCTIONING DRAINAGE TUBE

| Type of drainage tube | No. |
|---|---|
| Catheter | 20 |
| T-tube | 6 |
| Not stated | 3 |

A catheter was used 3 times as often as a T-tube in the whole series.

| Type of incision for drainage | No. |
|---|---|
| Through wound | 19 |
| Through stab wound | 8 |
| Not stated | 2 |

Operative wound drainage was used twice as often as stab wound drainage in the whole series.

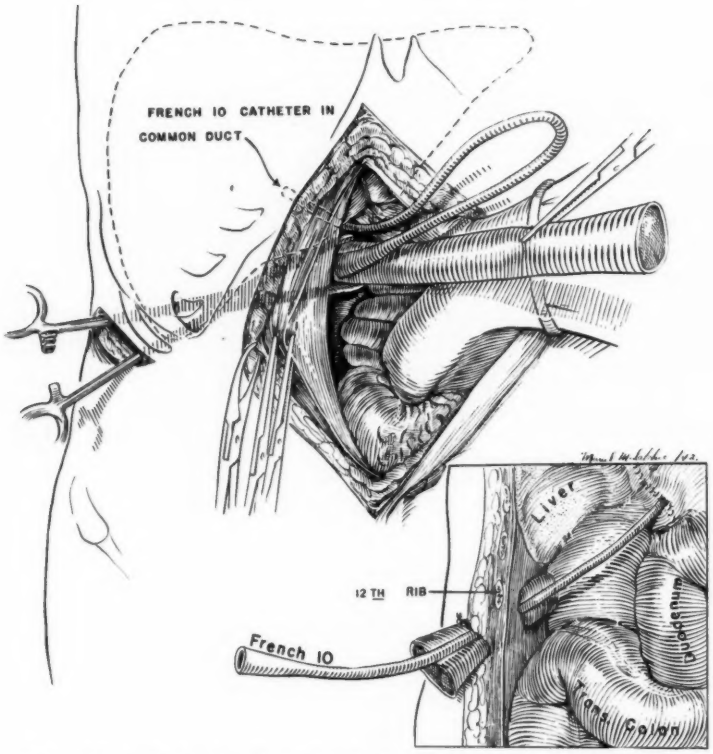



Fig. 2. Schematic drawing illustrating the introduction of common duct drainage tube and cigarette wick through a stab wound in the right flank well below the 12th rib. This must be done under vision, since it is possible to damage the hepatic flexure of the colon or pull omentum through the wound if care is not taken in the maneuver. The inset shows the proper location of the tubes with the abdominal wall cut away.

relatively smooth convalescence while the others were stormy. The type of drainage tube and the type of wound closure (Table VI) had no apparent influence on the malfunction of the tube.

Of the 4 fatal cases of bile peritonitis, 2 had stab wound drainage and 2 were drained through the wound. This amounts to twice as many deaths from bile peritonitis when stab wound drainage was used. We stress this point in spite of the small number of cases, because we believe that others may avoid some of our earlier difficulties. There are a variety of technical errors, which explain failure of the tube to function. These are: kinking of the tube, ligature or stitch around the tube, pulling of end of the tube from the duct, and adhering together of the sides of the tube. The importance of using tubes of fresh rubber cannot be overemphasized. This is brought out by an unfortunate death in the series. In removing a tube on the 10th day of uncomplicated convalescence, the tip distal to the fixation stitch remained in the common duct. This was later removed by laparotomy following which the patient died of bronchopneumonia.

We now follow the rule and strongly urge that every common duct tube drain bile while the patient is on the operating table and if bile does not continue to drain, the patient is returned to the operating table and a tube is

made to function. This should be done the day of the original operation in order to save the patient from the effects of bile spreading throughout the abdominal cavity. If one waits until the signs of bile peritonitis are apparent, the risk of fatal outcome is very great. In our series, 22 per cent succumb, while McLaughlin reports the mortality to be 2 or 3 times this figure.

The amount of daily bile drainage was tabulated not only to determine the average normal output and to determine the significance of output of large amounts but to find out the relation of the size and the type of drainage tube to this amount.

The most frequently used drainage tube was a No. 10 French whistle-tipped catheter and there was no apparent difference in the amount of bile drainage when the tip was placed up toward the liver or down toward the duodenum; although we believe that small ducts should have the catheter pointing toward the liver (1). The usual case with a smooth convalescence averaged 8 to 10 ounces of bile in 24 hours through a No. 10 catheter. More than 16 ounces in 1 day was unusual and an output of 18 ounces or more for more than 1 day invariably meant residual pathology. Larger catheters and T-tubes averaged 2 to 4 ounces more bile drainage daily. The position of the tube through the abdominal wall (stab or wound drainage) made no apparent difference in the amount of external biliary output.

When a No. 10 catheter was used and removed on the 10th day, biliary drainage practically always ceased within 48 hours and the wound was usually dry in 24 hours. With larger catheters, drainage was prolonged after removal and even more so after the use of a T-tube. The curves of postoperative hospital stay of patients in the Massachusetts General Hospital with catheter and T-tube drainage are shown in Graph 1. The average postoperative stay for patients drained with a catheter was 16.0 days and those with a T-tube 21.7 days. This difference is striking and seems to be chiefly due to prolonged drainage of bile following removal of the T-tube. However, wound sepsis also is an important factor as most of the T-tubes were brought out with

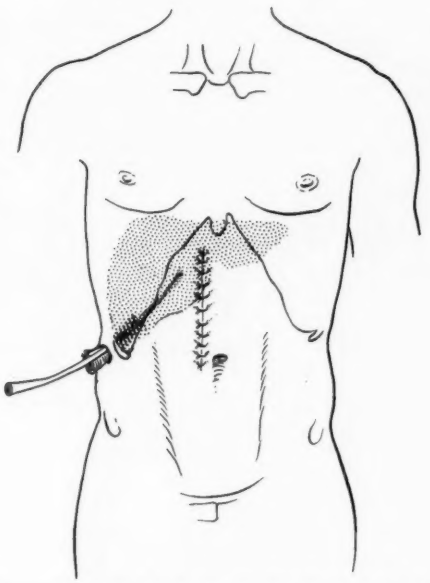


Fig. 3. Schematic drawing illustrating the final situation. The wick and the tube should be sutured to the skin with separate nonconstricting silk stitches.

the abdominal drain through the operative incision. It must be recorded that in a few instances, T-tubes were used when prolonged external drainage of the common duct was desired.

Anesthesia was used 4 times for the removal of a T-tube and in no instance for the removal of a catheter. We have felt that 10 days was a sufficient length of time for the tube to remain in the duct in those patients who have had careful graded dilatation of the papilla of Vater. We have removed the cigarette wick on the 10th day and the catheter as soon afterward as the No. 00 chromic catgut suture, holding it into the common duct, would let go. If a separate stitch is used for this fixation, the catheter comes away with greater ease than when the fixation stitch is a part of the continuous suture closing the incision in the duct.

Reaction following removal of the drainage wick occurred in 19 individuals; twice when a stab wound was used and 17 times when the wick was brought out through the operative wound. The average oral temperature elevation was 101.2 degrees. The chart was flat in

14 instances by 48 hours, 3 by 72 hours, and the remaining 2 by 96 hours. It would seem that the removal of a short dependent wick placed away from the operative field is followed by less reaction than is the longer one brought upward through the operative incision. The removal of the shorter wick also gives less discomfort to the patient. There are other logical reasons for using this short wick through a lateral incision directly into the subhepatic space. As Morison originally pointed out, this is the fossa which collects the secretions from the field of operation. All fluid escaping from the right side of the water shed, formed by the spinal column, must gravitate to this region before it can escape either to the outside or into the various intra-abdominal areas. One may have the theoretical objection that a wick so placed would increase the danger of infecting the fluid carried above the liver by the effect of respiration. It seems to us that the early provision for escape of fluid, as it collects, is actually a safeguard against an accumulation between the liver and the diaphragm.

As a matter of fact, our data seem to indicate that adequate drainage to the outside is accomplished by the long wick introduced into the subhepatic fossa and brought out through the operative incision. This drainage is at first by capillary attraction and by the time this action is lost, a sinus tract is established. One of our chief objections to the long wick is that with postoperative distention the drain sutured to the skin may well be lifted out of its dependent position. If this occurs, or if the wick is placed to the operative field, disabling adhesions between the site of operation and the duodenum may occur.

We do not think one should use the lateral stab wound drainage in every instance. We have avoided its use in patients with a very thick abdominal wall. In such individuals, one is apt to find a wide flaring costal angle and these are best operated upon through some modification of the transverse approach. In secondary operation on the common duct, one is apt to find the subhepatic space obliterated by adhesions which we believe should usually be left alone, thus making it more logical to bring out the drains through the operative incision. This is also true in cases of common duct repair, especially if the repair is made over a T-tube. We have found it difficult to establish an external biliary fistula that does not follow the liver sulcus to the surface in the region of the attachment of the ligamentum teres.

## SUMMARY AND CONCLUSIONS

When the common duct has been opened, drainage through a suitable tube to the outside should be routinely established. Tight suture of the incision in the duct is difficult to accomplish.

Bile peritonitis carries a high mortality rate and can be greatly diminished by proper drainage of the region of operation.

Tubes should be functioning before the abdominal incision is closed. If function ceases, this should be corrected before the signs and symptoms of bile peritonitis are evident.

Whistle-tip catheters are adequate for drainage of the common duct, particularly if the papilla of Vater has been gradually dilated to 7 millimeters. This type of tube should be pointed toward the liver if the duct is small, since the open end will allow for easier escape of bile through the tube. Such a tube can be removed without injuring the suture line in the duct, and there is a minimal amount of drainage after its removal.

In the average case with a vertical paramedian incision, one may reduce the morbidity caused by wound infection, dehiscence, and hernia in scar by providing a carefully placed lateral stab wound through which the drains may be brought.

## REFERENCES

1. ALLEN, ARTHUR W. Surgery, 1940, 8: 188–203.
2. ALLEN, ARTHUR W., and WALLACE, RICHARD H. Am. J. Surg., 1935, 28: 533–561.
3. Idem. Ann. Surg., 1940, 111: 838.
4. MCLAUGHLIN, JR., CHARLES W. Ann. Surg., 1942, 115: 240–249.
5. MORISON, RUTHERFORD. Brit. M. J., 1894, 2: 968–971.
6. WALLACE, RICHARD and ALLEN, ARTHUR W. Arch. Surg., 1941, 43: 762–772.

# ILEUS ASSOCIATED WITH EDEMA OF THE BOWEL

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ATTENTION was directed to the problem of ileus associated with edema of the bowel by a small group of cases in the so called paralytic obstructions in which the Miller-Abbott tube failed to pass along the small bowel at the usual rate of speed. Abbott had previously observed a patient in the uremic state with abdominal distention who failed to advance the tube. This was apparently caused by the depressed motor activity of the small bowel.

In the series of cases with acute intestinal obstruction reported by McIver from the Massachusetts General Hospital between 1918–1927, inclusive, 9 were classified as functional obstructions because no recognizable pathology was found at autopsy. These cases occurred in the very young or aged patients, and the functional disturbance of the bowel was attributed to their poor constitutional state.

Jones and Eaton discuss the effect of edema on the gastrointestinal activity in their report on postoperative nutritional edema observed in a variety of surgical patients. The factors responsible for the edema, mainly the low plasma protein concentration because of preoperative starvation and excess intravenous saline after operation, were fully appreciated by these authors.

Ravdin and his coworkers (9, 10, 11) pursued the problem further and demonstrated that the gastric emptying time, as measured by the water barium meal, was prolonged in dogs and patients when the serum protein concentration was lowered. This fact was true in both the intact stomach and after shortcircuiting operations.

In further studies by this group (Borden, Thompson, Ravdin and Frank(4)), the small bowel emptying time of dogs was seen to increase as the serum protein concentration was reduced by repeated plasmapheresis.

Of the cases of small bowel obstructions at the Presbyterian Hospital during the past 4 years, a group of 51 cases was classified as "paralytic" because the Miller-Abbott tube failed to demonstrate a mechanical obstruction during the process of deflation. Paralysis or inhibition of normal bowel motility was apparent in a few cases with known lesions of the spinal cord and retroperitoneal space. The Miller-Abbott tube advanced slowly along the bowel in the process of deflation, and repeated daily studies with barium injected through the tube showed only dilated loops of atonic bowel distal to the advancing tip of the tube (Table I). Seventeen cases associated with edema also exhibited this marked depression or inhibition of small bowel activity. These cases, associated with edema of the bowel, required an average of 6.2 days to advance the Miller-Abbott tube along the entire length of the small bowel. In contrast, 26 cases attrib-

TABLE I.—SMALL BOWEL OBSTRUCTIONS—PARALYTIC TYPE

| Cause of obstruction | Number of cases | Total | Average time for Miller-Abbott tube to traverse small bowel—days |
|---|---|---|---|
| Spinal cord lesions | | 3 | 12 |
| Ascending transverse myelitis | 2 | | |
| After spinal pontocaine | 1 | | |
| Retroperitoneal lesions | | 3 | 5.4 |
| Hemorrhage from abdominal aneurysm | 1 | | |
| Traumatic rupture of ureter | 1 | | |
| Operative trauma and hemorrhage | 1 | | |
| Associated with edema of the bowel | | 17 | 6.2 |
| After gastrointestinal surgery | 10 | | |
| Liver disease | 2 | | |
| Nutritional deficiencies | 2 | | |
| Uremia due to renal failure | 2 | | |
| Extensive cutaneous burns | 1 | | |
| Operative trauma | | 26 | 2.1 |
| After extensive pelvic surgery | 17 | | |
| After abdominal explorations | 4 | | |
| After resections of colon or rectum | 5 | | |
| Bronchopneumonia | | 2 | 2.5 |
| Total cases | | 51 | |

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Read before the Forum on Fundamental Surgical Problems at the Clinical Congress of the American College of Surgeons, Boston, Massachusetts, November 7, 1941.

Aided by a grant from the Josiah Macy, Jr. Foundation.

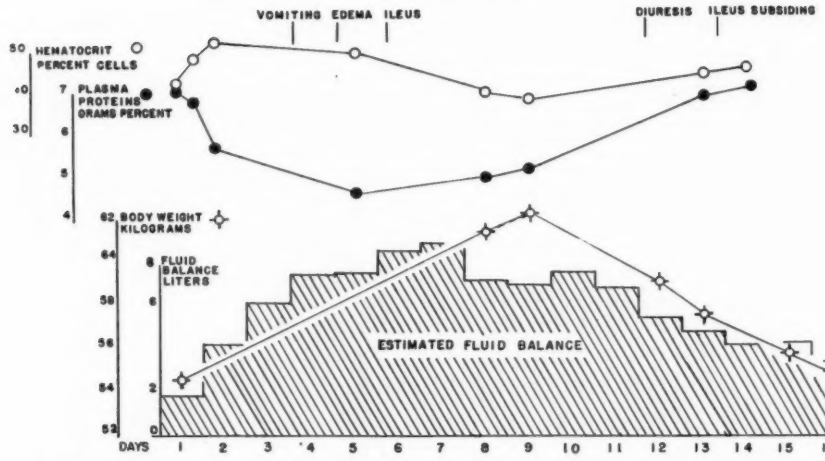

VOMITING EDEMA ILEUS
DIURESIS ILEUS SUBSIDING
HEMATOCRIT PERCENT CELLS
PLASMA PROTEINS GRAMS PERCENT
BODY WEIGHT KILOGRAMS
FLUID BALANCE LITERS
ESTIMATED FLUID BALANCE
DAYS 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16

Chart 1. The typical course of the changes in the plasma protein concentration, hematocrit, and total body weight during the development of ileus associated with edema of the bowel following an extensive cutaneous burn.

uted to operative trauma required an average of only 2.1 days to pass the tube into the cecum.

The typical cases in the group associated with edema of the bowel were similar to the cases stressed by Ravdin and Rhoades (10) and Jones and Eaton in gastric cases. Ravdin's statement that "too much emphasis has been placed on the water and salt replacement of the surgical cases and too little on the mechanism involved in keeping the fluids within the blood vessels" is well demonstrated in these cases.

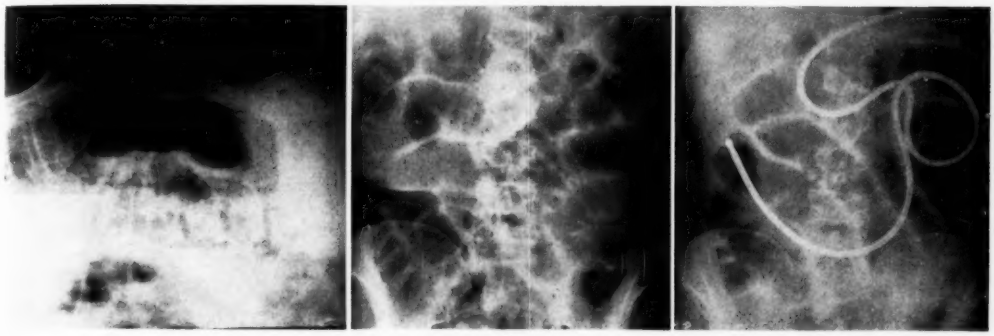
### ILLUSTRATIVE CASES

CASE 1. Male, aged 51 years (Chart 1) with extensive cutaneous burns who was under detailed study for changes in fluid distribution. The estimated positive fluid balance in these charts is calculated by subtracting the total fluid output (urine and vomitus) plus an additional 1500 cubic centimeters daily for insensible fluid loss from the total fluid intake. These figures parallel fairly well the actual changes observed in the total body weight. It may be seen that there was a gain in body weight of over 8 kilograms during the first 6 hospital days. The typical rapid fall in plasma protein concentration accompanied by a rapid rise in the hematocrit was observed during the first few days. Weech, and Drew, Scudder, and Papps have emphasized that this type of blood picture will not prevent edema formation even in the presence of hemoconcentration. When vomiting begins, the usual treatment is directed to water and salt replacement which of course only increases the edema (Beard and Blalock).

The abdominal roentgenograms (Fig. 1) in this case (and in others in this group) showed the typical picture of ileus with dilated loops of small bowel with fluid level formation in the lateral decubitus positions. Small bowel intubation started on the 6th hospital day relieved the symptoms of nausea and vomiting, but the tip advanced only a few feet during the next 2 days. All intravenous therapy was discontinued except plasma. The Miller-Abbott tube passed rapidly into the transverse colon during the next 12 hours as diuresis began and distention disappeared.

CASE 2 (Chart 2). A female, aged 63, showed the same typical picture following a partial colectomy for carcinoma of the sigmoid. Twenty liters of normal saline were administered during the 5 days following operation. Increasing abdominal distention and vomiting began on the 3d postoperative day. A low plasma protein concentration and high hematocrit were found at this time. Several whole blood transfusions during the next 2 days failed to relieve the distention or cause a diuresis. A cecostomy done on the 5th postoperative day failed to function. Two liters of ascitic fluid were present at the second operation, and the bowel was described as edematous. Small bowel intubation started on the evening of the 7th postoperative day delivered 11 liters of fluid from the upper gastrointestinal tract during the next 36 hours. Six additional days were required for the Miller-Abbott tube to reach the cecum. At this time a mild diuresis began, and the normal bowel function was re-established.

The abdominal roentgenograms (Fig. 2) illustrate the chief difficulty encountered in these cases. The tip of the Miller-Abbott tube can be easily passed into the duodenum with-



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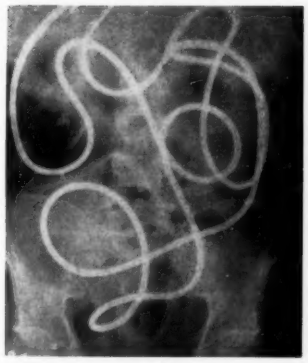

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Fig. 1. Ileus associated with edema of the bowel following an extensive cutaneous burn. Abdominal roentgenograms in the lateral decubitus position. a, Showing dilated loops of small bowel with fluid level formation; b, plain abdominal roentgenogram just prior to small bowel intubation; c, showing the slow progress of the Miller-Abbott tube and deflation during the first 2 days of intubation; d, 12 hours later after 1000 cubic centimeters of plasma intravenously. The distention has disappeared, and the tube advanced to the transverse colon.

out the usual difficulty encountered at the pylorus in cases with obstructions. After the balloon has been inflated in the duodenum, having passed the pylorus, the tube is usually fed into the stomach at the rate of approximately 6 inches every 1 or 2 hours. In these cases, however, the tip fails to advance at the usual rate of speed and the excess tubing accumulates in the stomach or prolapses extra loops into the duodenum (Fig. 2b). This may cause sharp angulations in the tube which occlude the lumen and interfere with suction.

## EXPERIMENTAL

In acute experiments on 4 normal dogs we have observations that support the results reported by Borden and his coworkers (4) from prolonged studies on dogs with reduced plasma protein concentration (Chart 3). Motility in the small bowel was recorded from a balloon attached to a water manometer. As the plasma proteins were rapidly depleted by plasmapheresis and by the injection of additional normal saline, both the tone and peristaltic activity of the small bowel were depressed. In these experiments the hematocrit and blood pressure were maintained at almost normal levels although the heart rate was usually increased.

It should be emphasized that this method of studying small bowel activity will give misleading results unless done carefully. The balloon must be inflated for only a short period of time and with only small amounts of air. Otherwise edema of the bowel will result even in the normal dog. Furthermore, the injection of saline or rapid bleeding may cause a momentary increase in the motor activity of the bowel.

In the clinical cases (Table I) gross edema of the bowel was described either at operation or at proctoscopic examination. In the acute

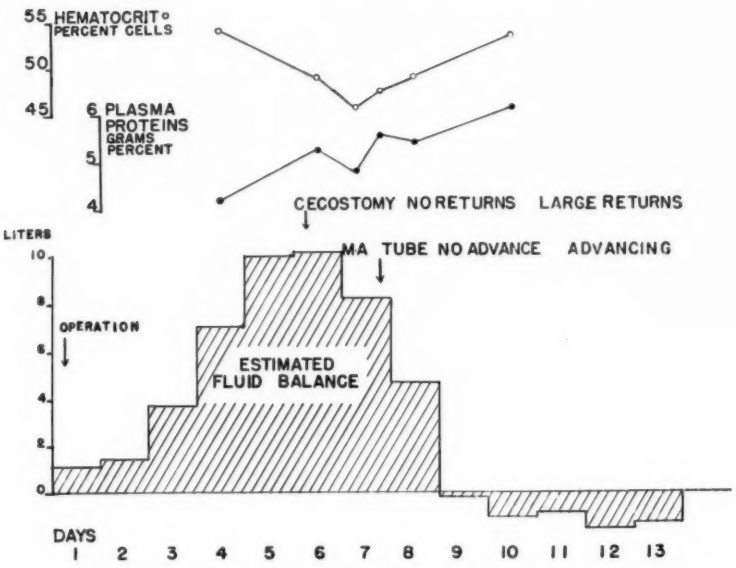



Chart 2. The effect of excess intravenous saline on the plasma protein concentration, hematocrit, and positive fluid balance following partial colectomy for carcinoma of the sigmoid.

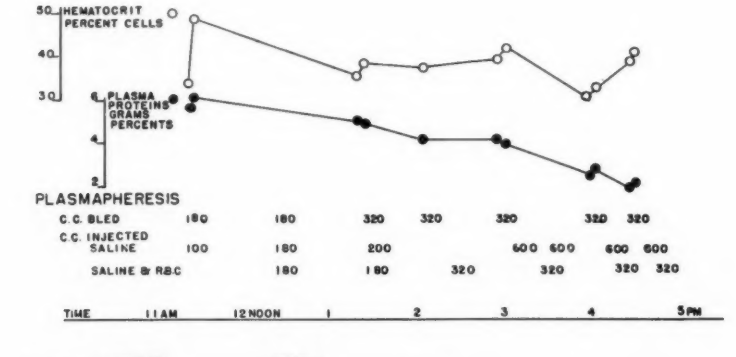
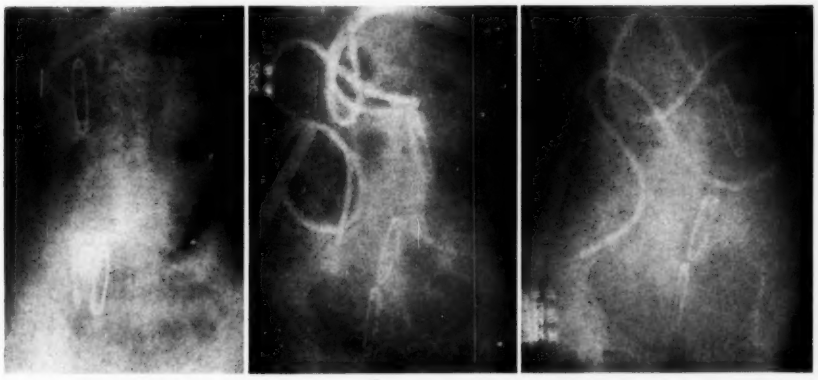



Chart 3. The effect of rapid plasmapheresis on the plasma protein concentration, hematocrit, and intestinal motility in the experimental animal.



a b c

d

Fig. 2. Ileus associated with edema of the bowel after partial colectomy for carcinoma of the sigmoid. a, Plain abdominal roentgenogram just prior to cecostomy; b, showing the slow progress of the tube during the first 2 days of small bowel intubation. Continued slow progress of the tube on the third, c, and fourth, d, days of intubation. Complete deflation required 6 days.

experiments, however, the bowel was paler than normal but not grossly edematous. The inadequacy of conclusions drawn from gross observations was emphasized by LePore (1932) after his careful studies on the water and salt content of the skin and various organs of the body in normal dogs and dogs rendered edematous by starvation and repeated plasmapheresis. When gross edema was observed in the skin of the hind legs, the water content increased from 58.7 per cent water in the normal to from 81.40 to 88.45 per cent water in the edematous state. The normal intestine, however, contained 75.70 per cent water and increased to only 81.75 per cent water in the edematous state.

## OBSERVATIONS

It would appear that the association between depressed motor activity and edema of the bowel is not caused by the poor constitutional state of the patients. Although the patients with ileus ascribed to operative trauma (Table I) were in as poor general condition as the others, the deflation was accomplished rapidly with the Miller-Abbott tube. Bisgard has gone so far as to propose that the term paralytic ileus should not be applied to the cases of ileus usually attributed to operative trauma, because he could demonstrate vigorous peristaltic activity in these patients immediately after operation. The present writer also believes that in those cases in which the ileus is ascribed to operative trauma, it is probably a result of mechanical obstructions caused by delicate adhesions which disappear during the process of deflation. We have retained the accepted term, however, until positive evidence can be presented. Bisgard's observations support the opinion that the edema

is caused by the low plasma protein concentration and by excess intravenous saline rather than being the result of lymph stasis on the basis of operative trauma and consequent inactivity of the small bowel.

We are purposely avoiding a discussion of the factors responsible for the gaseous distention in these cases. It is a well known fact that many patients with widespread edema of the bowel and undoubtedly marked depression of intestinal activity have only mild difficulty from gaseous distention of the bowel. The important fact for the surgeon to note is that true inhibition of the motor activity of the bowel is present in only two types of cases: those associated with lesions of the spinal cord or retroperitoneal space, and those accompanied by edema of the bowel. In the latter group, rapid deflation can be accomplished by ridding the bowel of edema and restoring small intestinal activity.

## CONCLUSIONS

Small bowel motility has been found markedly depressed in cases with ileus associated with edema of the bowel.

In most cases the edema appeared to aggravate existing partial mechanical obstructions of the bowel (Case 2). In a few cases the edema was the only known etiological factor present (Case 1).

Therapy directed to fluid and salt replacement will increase the edema as long as the plasma protein concentration remains at edema level.

Therapy directed toward raising the plasma protein concentration will restore small bowel activity and aid in the deflation of the patient.

## REFERENCES


1. Abbott, W. Osler. Personal communication.
2. Beard, J. W., and Blalock, A. J. Clin. Invest., 1932, 11: 249.
3. Bisgard, J. D. The effect of hot and cold applications to the abdominal wall and also hot and cold fluids administered by mouth on gastric and intestinal secretory and peristaltic activity. In press.
4. Borden, R. P., Thompson, W. D., Ravdin, I. S., and Frank, I. L. Surg. Gyn. Obst., 1938, 66: 819.
5. Drew, Charles R., Scudder, John, and Papps, Jean. Surg. Gyn. Obst., 1940, 70: 859.
6. Jones, C. M., and Eaton, F. B. Arch. Surg., 1933, 27: 159.
7. LePore, M. J. Arch. Int. M., 1932, 50: 488.
8. McIver, Monroe A. Acute Intestinal Obstruction. New York: Paul B. Hoeber, Inc., 1934.
9. Mecray, M. P. Jr., Borden, R. P., and Ravdin, I. S. Surgery, 1937, 1: 53.
10. Ravdin, I. S., and Rhoades, J. E. Surg. Clin. N. America, 1935, 15: 85.
11. Ravdin, I. S., Pendergrass, E. P., Johnston, C. G., and Hodes, P. Am. J. Roentg., 1937, 35: 306.
12. Ravdin, I. S. Ann. Surg., 1939, 109: 321.
13. Weech, A. A. Quoted from a discussion at the New York Academy of Medicine, 1939.

# INSULT TO THE TESTICLE IN HERNIORRHAPHY

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OF the last hundred patients operated upon for inguinal hernia at The Mason Clinic, we have had but two who developed immediate, detectable, postoperative testicular swelling. These cases are reported herewith, as it is believed that their course and treatment may be instructive. That we have been fortunate is suggested by comparison with the carefully reported series of 150 patients operated on for inguinal hernia at Lahey Clinic (1), 6.7 per cent of whom developed shortly after operation some evidence of atrophy of the testicle on the side operated upon. There had been no previous disorder in any of these organs.

In a study of the case histories of 1,093 patients operated on for inguinal hernia, Erdman found an incidence of 13.1 per cent of postoperative tumefactions in the scrotum. In his series, 4.6 per cent developed early hyroceles which contained from 20 to 60 cubic centimeters of clear yellow fluid. Outside the hydroceles, this author classified other tumefactions as distention of the veins in the pampiniform plexus, thrombosed veins, thickening of the tunica, hematomas, and epididymo-orchitis. It is interesting to observe that the majority of those classified as hematomas and epididymo-orchitis subsequently developed atrophy of the testicle. In this group, 11 patients, or 1 per cent, complained of pain in the groin or scrotum for a period of from 3 months to 2½ years, and the author believes that one-half of these probably had nerve involvement as the etiological factor. Of these, 1.5 per cent developed postoperative atrophy of the testicle.

In a series of 1,500 cases, Huston found only 3 which showed evidence of postoperative atrophy of the testicle. These were observed early in the series, before his operative technique was modified to give less compression to the cord. The literature contains reports of cases of frank necrosis of the testicle following herniorrhaphy, and even operation on and about the neck of the urinary bladder in some instances has been followed by gangrene of the testicle.

Many statistical follow-ups on inguinal herniorrhaphies mention the most remote complications, yet fail even to consider damage sustained by the testicle.

## PSYCHIC EFFECT

The occurrence of any complication that involves the genital organs, or even their immediate vicinity, has a particularly devastating effect upon the morale of the patient. In the male, painful or swollen testicles, atrophy of the organ, discoloration of the scrotal skin, tumefaction of the scrotum and numbness of the skin of the scrotum, medial thigh, or pubic region create mental unrest in those unacquainted with the nature of the condition. This is especially true of the younger adult, whose apprehension of sterility or even impotence may be deep in his mind. It is strange how readily even an extragenital complication may be interpreted as a probable cause for impaired or lost sexual function. The surgeon must be aware of this fact, though the very nature of the patient's concern is such that he makes little or no mention of it.

## ANATOMY

Familiarity with the structures in and around the inguinal canal is required for appreciation and understanding of the sequelae of hernial repair.

The arterial supply to the testicle comes almost exclusively from the internal spermatic vessel in the cord. A small branch of the deep epigastric artery passes through the canal, as does a division of the (vas) deferential artery, but the supply of blood to the testicle by these channels is negligible. Any process which occludes the spermatic artery will certainly involve these smaller vessels. The venous return courses, for the most part, in the pampiniform plexus about the cord.

Running with the cord in the canal are two nerves, chiefly sensory, namely, the ilioinguinal and external spermatic nerves. The ilioinguinal nerve supplies the skin of the upper medial part of the thigh and the root of the penis and scrotum. A few fibers of this nerve, supplying part of the internal oblique muscle, usually split from the main bundle far enough proximally to be out of the field of danger. The external spermatic is a branch of the genitofemoral nerve, and, besides giving motor fibers to the cremasteric muscle, supplies sensory fibers to part of the skin of the scrotum. Just above the inguinal canal and running parallel to it, beneath the aponeurosis of the external oblique, is the anterior cutaneous branch of the iliohypogastric nerve. Destruction of this leaves an anesthetic area of skin on that side, superior and lateral to the symphysis pubis.

### PATHOLOGY

The most common disorder of the testicle following inguinal herniorrhaphy is passive congestion from obstructed venous return. It is strange, but unfortunate for the surgeon that the reactions of the tissues, in different subjects, vary with identical operative procedures. In some, even with most gentle manipulation, local vasoconstriction is marked and there is probable circulatory embarrassment to the parts supplied and drained, while in other subjects, necessary vigorous manipulation leaves no demonstrable after-effects.

Passive congestion of the testicle can be responsible for the following conditions:

1. Dilatation of the veins in the pampiniform plexus.
2. Hydrocele from passive transudation.
3. Lowered tissue resistance and, hence, active infection from a dormant local condition or a circulating organism that ordinarily would not find such a favorable medium.
4. Lastly, but most important, from our viewpoint, an increased intratesticular tension which may become severe enough to cause pressure necrosis of the parenchyma and ultimate atrophy of the testicle. It is hard to believe that passive congestion alone can cause this unless the venous return is blocked completely. The most likely explanation, in our opinion, is that tension sufficient to enlarge the testicle is the result of passive congestion plus a subacute inflammatory process. Under ordinary circumstances, exudation produces much more tension than pure transudation. This belief is well supported by the observation of Erdman that those cases that went on to atrophy had been diagnosed either as epididymo-orchitis or hematoma.

Hertzler, in his monograph on the surgical pathology of the genitourinary organs, states that the four most common causes of atrophy of the testicle are: mumps, herniorrhaphy, trauma, and varicocele.

In an interesting study of circulatory changes in the testicle by Iwasita, the following observations, with rabbits and dogs as subjects, were made:

A. With complete occlusion of all of the spermatic veins and release after 24 hours, study of the tissue of the testicle showed slight passive congestion, and, 5 days after the return of the circulation, there was proliferation of the interstitium with slight hemorrhagic infarction, but the parenchyma was only slightly altered after this temporary congestion.

B. After occlusion of the veins and vas deferens at the same time and release of the ligature in 24 hours, slight necrosis of the parenchyma, interstitial hemorrhage, and moderate dilatation of the veins were found, and 5 days later the testicle showed complete hemorrhagic infarction.

C. When all the structures of the cord were tied off for a period of 5 hours and then released, there was practically no destruction to be found in the testicle after 28 days.

D. When all the structures of the cord had been ligated for a period of 10 hours and then released, complete degeneration of the parenchyma and fibrous proliferation throughout was noted in sections of the testicle 45 days later.

Viewed in the light of the knowledge gained by the aforementioned experimental work, it behooves us to keep careful watch for postoperative swelling and to institute treatment promptly when the integrity of a testicle is threatened. We could find no report of investigation as to the relation between the ac-

tual amount of swelling of a testicle, or the length of time that any degree of enlargement could be allowed to continue, with a prognosis as to permanent damage to the testicle.

### TREATMENT

Very little can be found in the literature on the surgical procedure for preventing postoperative atrophy of the testicle. Measures have been proposed to relieve the tension developing in the orchitis of mumps.

The treatment is first of all preventive, and, in herniorrhaphy, the requisites for this are the establishment of an adequate sized aperture for the passage of the cord, reduction of the bulk of the cord (Halsted), and minimizing the trauma to the tissues. Careless reduction of the bulk of the cord has been reported as a probable cause for postoperative atrophy of the testicle.

Curative treatment must aim at exploration of the repair and widening of the passageway for the cord or at dividing the capsule of the testicle to forestall possible pressure necrosis. This latter method was our choice in 1 of our 2 cases when the testicle had enlarged painlessly to a size one and one-half times its normal 24 hours after operation.

As to the technique of incising the capsule, we used a straight incision from pole to pole on the exposed surface of the organ (Fig. 1). This method insures the greatest possible relief of capsular restraint. The immediate evagination of the parenchyma as the incision is made, we feel, is an argument for, rather than against, this method. Multiple slit incisions have been used by others (Ballenger, Smith, and Elder in the publications already quoted), and in this way they release much of the internal pressure and still retain capsular tissue throughout. Hot wet packs are applied after the closure, and we used one small Penrose drain in the incision. In our case, local infiltration anesthesia was used with satisfactory results.

### CASE REPORTS

W. C. (No. A-52928), aged 40 years, entered the Clinic October 4, 1938, with a history of having noticed a rather severe strain in both groins while playing golf a few days before his entrance. Physical examination showed bilateral inguinal hernias which were shown at surgery to be direct.

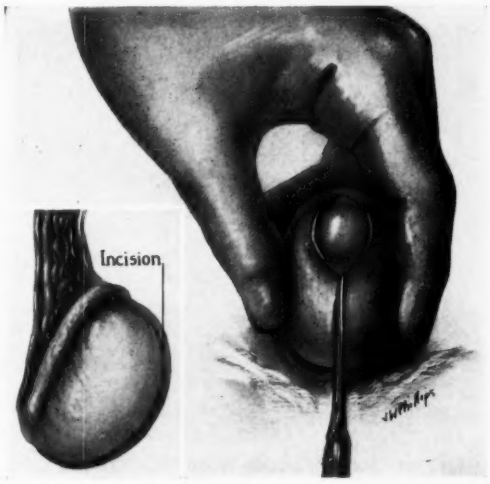


Fig. 1. A continuous straight incision from pole to pole is made. The site of choice is directly opposite to the root of the organ.

A modified Bassini herniorrhaphy was done on each side, and fascial transplants were employed to bind the conjoined tendon and internal oblique muscle to the shelving edge of Poupart's ligament. The patient developed an upper respiratory infection and was troubled with gas pains. About 12 hours after operation, swelling of the right testicle was noticed. The testicle enlarged to one and one-half times its former size. Two months later, atrophy of the organ was observed; and in 4 months, it was no more than 1.5 centimeters in diameter.

L. R. (No. A-15051), aged 47 years, came to the Clinic September 24, 1940, with a history of having noticed pain in the right groin upon coughing 4 days before.

Physical examination showed a right indirect inguinal hernia, 3 centimeters in size, which was reducible. The left inguinal region was normal. Two months later, a Bassini herniorrhaphy was done. A "pantaloon" was encountered, and the herniated sac was seen to be of the direct type.

Repeated observations during the following 24 hours showed progressive, painless enlargement of the testicle, and at the end of this 24-hour period operative intervention was decided upon. Incision of the capsule, as described, was done. Further scrotal swelling and discoloration ensued. The swelling had subsided appreciably at the end of 2 weeks. Subsequent examination at the end of 6 weeks showed no evident enlargement of the scrotum or testicle. Convalescence was otherwise uneventful, and a low grade fever that had been present with the postoperative swelling quickly subsided.

Examination of this man 2 years later showed no discernible abnormality of the involved testicle de-

spite the fact that it had developed, after operation, sufficient internal pressure to enlarge it to one and one-half times its normal size.

## REVIEW

These two have been the only cases of demonstrable swollen testicle complicating this series of 100 inguinal herniorrhaphies. In the one, we did nothing, and a marked atrophy followed within 4 months, while in the other a prompt decompression of the testicle by incision of its capsule resulted in immediate extreme swelling but ultimate return to normal size with no atrophy in a 2 year period.

Some degree of atrophy may have occurred in others, but severe atrophy is not to be expected when manifestations cannot be noticed while the patient is in the hospital. And, further, we should expect to hear from our patients who have suffered marked atrophy.

## CONCLUSION

We wish to emphasize finally the following points:

1. The importance of examining the testicles and scrotum frequently during the first 48 hours after herniorrhaphy.

2. The value of describing on a permanent record the relative size of the two testicles before or at the time of operation.

3. The expediency of prompt decompression in the event of postoperative swelling, either by loosening the repair above or, as here reported, by releasing the capsular restraint.

## REFERENCES

1. Cattell, R. B., and Anderson, C. N. England J. M., 1931, 205: 430–432.
2. Elder, O. F., and Ballenger, E. G. J. Am. M. Ass., 1920, 75: 1257.
3. Erdman, S. Ann. Surg., 1923, 77: 171–189.
4. Iwasita, K. Jap. J. Derm. Urol., 1939, 45: 126–135.

# CLINICAL AND EXPERIMENTAL OBSERVATIONS ON THE USE OF CORPUS LUTEUM EXTRACTS IN OBSTETRICS

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WHEN a new therapeutic agent is proposed for any medical condition it is necessary for a certain period of time to elapse between the time of its introduction and that of its indorsement and adoption by the medical profession. A healthy skepticism prevails concerning new remedies which prevents their wholesale adoption until thoroughly tested.

The preparation of an organ extract by various methods results in the production of preparations of varying potency and content. The tendency at first is to assume that all of the results obtained by a given extract are due to a single hormone elaborated by the gland or tissue from which the extract is made. Later, as further evidence is accumulated, it may become evident that a given extract may contain substances having more than one action. This gives rise to confusion of thought and to the reports of conflicting evidence regarding the therapeutic activity of the preparations. For our purpose, therefore, in order to clarify our statements, we wish to state that in the active extracts from the corpus luteum which we have used, which have been purchased on the open market under various trade names, we have found that most of them contained a hormone which inhibited human uterine muscle contractions that had been stimulated by the injection of posterior lobe pituitary extracts (Fig. 5). Whether one wishes to designate such hormone by the word "progestin," or some other name, is beside the point. It is present in appreciable and usable quantities in both aqueous extract and in oil soluble extract preparations in varying amounts.

With the development of our knowledge of the hormones of the ovary has come a clearer conception of their chemical structure, their physiological activities, and therapeutic potentialities. The early separation of the estrogenic substance and its crystallization by Allen and Doisey, together with their description of the chemical formula placed this substance on a firm scientific foundation.

Attention was next directed to corpus luteum extracts. These were given the broad name of progestin because of the production of progestational changes in the spayed or virgin rabbit uterus. It was also found that they produced an inhibiting effect on uterine muscle contractions *in vitro* and *in vivo* (Figs. 1 to 5). More recently a purified product, progesterone, has been recovered from extracts of corpus luteum which will on injection into a rabbit produce progestational changes but which in our hands at least has very little uterine muscle contraction inhibiting power. Other less refined extracts of corpus luteum seem to contain this contraction inhibiting hormone which we think may be a hitherto unidentified hormone. For the sake of accuracy, therefore, we will speak in this paper of corpus luteum extracts in both water and oil solution, without attempting to define their chemical formula accurately since we feel that they contain the contraction inhibiting factor which this and previous studies (3) seem to show is the factor responsible for the beneficial results obtained clinically in the treatment of human abortion.

The use of extracts of corpus luteum in the treatment of both threatened and habitual abortion has progressed beyond the experimental stage, and has been accepted by many clinicians as a valuable adjunct to our therapeutic armamentarium. Numerous reports from various clinics attest the benefit derived from the proper use of this agent prophylactically as well as curatively after the onset of symptoms. The clinical impression of the therapeutic value of a drug or hormone, how-

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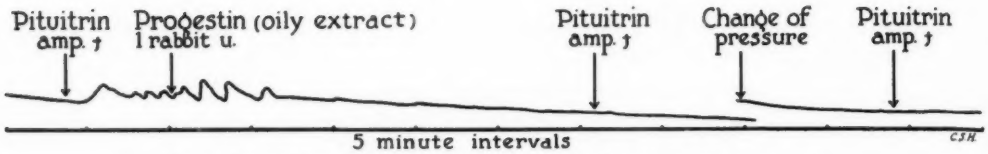


Fig. 1. Contractions stimulated by pituitrin, stopped by rabbit unit of progestin.

ever, is open to a certain amount of criticism because of the subjective character of the evidence presented. Nor do the results obtained from the use of a preparation in laboratory animal experiments convince a critical judge of its efficacy when used on the human. It was not until the action of corpus luteum preparations in stopping uterine contractions which had been induced by the injection of posterior lobe pituitary extracts in animals by Novak and Reynolds, and in human subjects by Falls, Lackner, and Krohn, had been clearly demonstrated by the intrauterine bag method of Moir, that the usefulness of these preparations in the treatment of abortion was established beyond any reasonable doubt.

Since demonstrating the pharmacological potency of these preparations in combating uterine contractions in human beings, and in order to convince ourselves that the clinical results obtained by Falls, Lackner, and Krohn in a series of 41 cases were not accidental, we have used it in a rather large series of cases at the Research and Educational Hospital, the Cook County Hospital, and in our private practice. The results obtained have been gratifying and confirmed our previous clinical impressions. Various preparations containing corpus luteum extracts have been used and their potency tested clinically as well as pharmacologically. We have thus obtained first hand information regarding the therapeutic potency of a considerable number of the preparations on the market. As might be expected a considerable difference in the activity of these preparations in inhibiting uterine contractions was noted. This probably explains the difference of opinion of certain observers regarding their clinical usefulness in the treatment of abortion.

In the last few years we have been especially concerned with the application of these preparations to the solution of other obstetrical problems dependent upon the contractility of the uterus. The principal conditions that we wish to discuss under this heading are placenta previa, premature detachment of the placenta, premature rupture of the membranes, and premature labor. Our observations have led us to believe that the use of corpus luteum extract injections at the proper time, the proper dose being used in all of these conditions, is of considerable value and marks the first attempt to correct the etiological factor concerned with the development of these serious obstetrical complications.

One of the next problems which caused difficulty in the clinical application of the hormone was the cost of production which made its use prohibitive for all but wealthy patients, when the treatment had to be continued for any considerable length of time. In searching for an answer to this problem, we decided to assay a water soluble corpus luteum extract which has been in general use for years. In spite of the fact that the hormones were thought to be contained only in oil extracts of corpora lutea, we were able to demonstrate that some aqueous preparations stopped uterine contractions induced by posterior hypophysis extract injections. We have found that, by using this material during

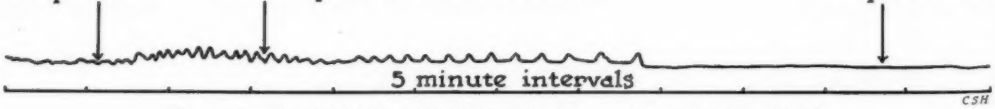


Fig. 2. Complete inhibition of pituitrin action by 10 cubic centimeters of lutein.

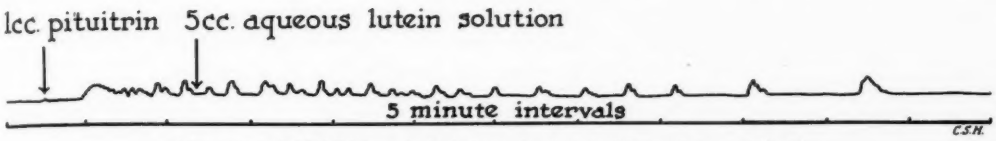


Fig. 3. Partial inhibition of pituitrin action by 5 cubic centimeters of lutein.

threatened abortion and as prophylactic treatment in cases of habitual abortion, we are able to minimize the expense of treatment without sacrificing safety. The aqueous solutions have the added advantage that they may be used intravenously in an emergency.

In order to obtain further information on the clinical value of corpus luteum extract in patients with threatened and habitual abortion, we have used an aqueous preparation[1] at the Cook County Hospital in the treatment of indigent patients entering this institution. The principles of management were the same as those laid down for our earlier work, and the management of the cases was closely followed by one of us (Dr. Benensohn). The work has been carried on now for a period of 2 years. A total of 272 cases have been treated, of these 217 could be classified as threatened abortion, and 59 as habitual abortion. An additional 59 cases were treated but not included in the series because the status of the pregnancy was unknown at the time the patient left the hospital or subsequently. The results can be seen in Tables I and II and Figures 1 and 2.

In the failure group the diagnosis was dependent upon gross or microscopic evidence of expelled products of conception. The routine of therapy instituted consisted of 3 cubic centimeters of aqueous corpus luteum extract administered intramuscularly every 4 hours for 6 doses, then 3 times per day for 2 days following which the dose was reduced to 2 cubic centimeters twice daily until discharged. The patient was required to be up and about for at least 2 days without bleeding, and free from pain before being discharged from the hospital. After discharge from the hospital, the treated patients were referred to the clinic for continuation of therapy and were instructed to return to the hospital if bleeding or pain suggested a recurrence of a threatened abortion. Thus, 65 cases herein presented were followed in the clinic. The remainder are known to have delivered viable pregnancies either at the Cook County Hospital or by other local institutions.

*Comments on failures.* Seventeen patients aborted while in the hospital despite large doses of aqueous corpus luteum extract, while in 2 cases only 6 cubic centimeters were administered. Three of these patients delivered macerated fetuses. Four patients aborted after discharge from the hospital. Three patients, 1 a diabetic, returned to the hospital as inevitable or incomplete abortions, and 1 patient expelled a dead 7 month previable fetus at home after being discharged from the hospital following 2 weeks of therapy.

Although the number of days of therapy is an excellent criterion of the amount of therapy necessary, it is noteworthy that in 91 of the 189 patients treated all bleeding and cramps subsided after receiving between 6 cubic centimeters and 9 cubic centimeters of aqueous corpus luteum extract.

*Control series.* There were 88 cases in which a diagnosis of threatened abortion was made on admission to the hospital. These were tabulated as to the duration of pregnancy when first seen in the hospital as follows:

[1]Lutein ampuls—a sterile aqueous extract of corpus luteum.

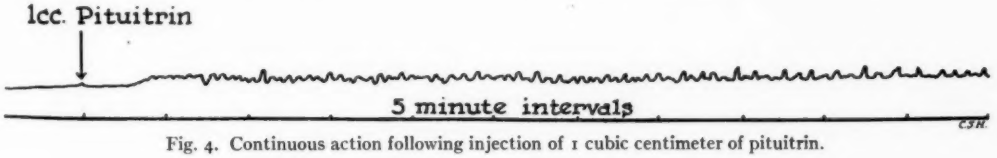


Fig. 4. Continuous action following injection of 1 cubic centimeter of pituitrin.

TABLE I.—THREATENED ABORTION IN WOMEN WITH HISTORY OF HABITUAL ABORTION—189 SUCCESSES, 28 FAILURES

| Duration of pregnancy when pain, bleeding or both began | 1–2 mos. | 3 mos. | 4 mos. | 5 mos. | 6–7 mos. | | | Total |
|---|---|---|---|---|---|---|---|---|
| | 58 | 52 | 34 | 28 | 17 | | | 189 |
| Amount of treatment based on hospital days | 2 days | 3 days | 4 days | 5 days | 6 days | 7 days | 8–10 days | |
| | 33 | 24 | 41 | 46 | 33 | 8 | 5 | 189 |
| Failures—duration of pregnancy | 1–2 mos. | 3 mos. | 4 mos. | 5 mos. | 6–7 mos. | | | |
| | 6 | 7 | 8 | 7 | | | | 28 |
| Per cent salvage | 83.5 | | | | | | | |

TABLE III.—RESEARCH AND EDUCATIONAL HOSPITAL—THREATENED ABORTIONS

| Duration of pregnancy when pain, bleeding or both began | 1–2 mos. | 3 mos. | 4 mos. | 5 mos. | 6–7 mos. | | | Total |
|---|---|---|---|---|---|---|---|---|
| | 42 | 40 | 28 | 27 | 69 | | | 206 |
| Amount of treatment based on hospital days | 2 days | 3 days | 4 days | 5 days | 6 days | 7 days | 8 or more days | |
| | 2 | 22 | 30 | 82 | 38 | 20 | 12 | |
| Failures—duration of pregnancy | 1–2 mos. | 3 mos. | 4 mos. | 5 mos. | 6–7 mos. | | | |
| | 8 | 0 | 4 | * 4 | 4 | 12 | | 28 |
| Per cent carried successfully to viability | 86.5 | | | | | | | |

Under 3 months, 44; 3 months to 18 weeks, 22; 18 weeks to viability, 22.

Therapy instituted in this series consisted of rest in bed, icebag to the abdomen, barbiturates or, in some cases, morphine sulphate. However, if the cases progressed to an inevitable abortion, quinine and pituitrin were administered in an attempt to hasten delivery In this entire series 55 patients, 61 per cent, completed the abortion; 33 cases, 39 per cent, were discharged from the hospital as still pregnant. Of the 55 patients that had aborted, only 6 pregnancies were beyond 18 weeks; 12 were estimated to be from 12 to 18 weeks pregnant; and 37 were pregnant less than 12 weeks.

In comparing the results in the 3 month period on corpus luteum extract, there were 15 failures in 112 cases, whereas, in the control group there were 37 failures in 44 cases.

The second series of cases (Table II) were cases of habitual abortion. All patients who gave a history of two or more abortions were placed in this group. Also cases with a history of one abortion but who in their present pregnancy presented a picture of threatened abortion such as spotting and cramp-like pains were also included in this group. Thus, 59 cases were placed in this group. Therapy consisted in most cases of at least 2½ cubic centimeters of aqueous corpus luteum extract two times per week. However, some of these patients did not appear for treatment but once a week. There were 51 successes and 8 failures.

During the same time we have treated at the Research and Educational Hospital and in our private practices 454 cases of which 243 were threatened abortions and 100 were habitual abortions. The results obtained in this group are shown in Tables III, IV, V, and VI.

It would seem then that in our hands, satisfactory results can be obtained in approximately 85 per cent of the cases, even though the County Hospital and Research and Edu-

TABLE II.—HABITUAL ABORTION—51 SUCCESSES, 8 FAILURES

| No. of previous spontaneous abortions | 1 abortion | 2 abortions | 3 abortions | 4 abortions | 5 or more | Total |
|---|---|---|---|---|---|---|
| | 16 | 18 | 9 | 3 | 5 | 51 |
| Duration of pregnancy when treatment started | 1–2 mos. | 3 mos. | 4 mos. | 5 mos. or later | | |
| | 13 | 15 | 12 | 11 | | 51 |
| Amount of treatment 1 injection—2 c.c. lutein | 5 to 9 ampuls | 10 to 19 ampuls | 20 to 29 ampuls | 30 to 50 ampuls | | |
| | 7 | 16 | 16 | 12 | | 51 |
| Failures—amount of treatment | 5–9 ampuls | 10–19 ampuls | 20–30 ampuls | | | |
| | 2 | 5 | 1 | | | 8 |

TABLE IV.—HABITUAL ABORTIONS

| Number of previous spontaneous abortions | 1 abortion | 2 abortions | 3 abortions | 4 abortions | 5 abortions | 6–10 abortions | over 10 | Total |
|---|---|---|---|---|---|---|---|---|
| | 20 | 22 | 4 | 5 | 0 | 4 | 3 | 58 |
| Duration of pregnancy when treatment started | 1–2 mos. | 3 mos. | 4 mos. | 5 mos. | 6 mos. | | | |
| | 12 | 31 | 10 | 4 | 1 | | | 58 |
| Number of 3 c.c. injections given | 5 to 9 ampuls | 10 to 19 ampuls | 20 to 29 ampuls | 30 to 49 ampuls | over 50 | | | |
| | 2 | 20 | 5 | 21 | 10 | | | 58 |
| Failures based on amount of treatment | 0 | 2 | 3 | | | | | 5 |

TABLE V.—THREATENED ABORTIONS—PRIVATE CASES

| Duration of pregnancy when pain, bleeding or both began | 1–2 mos. | 3 mos. | 4 mos. | 5 mos. | 6–7 mos. | | | Total |
|---|---|---|---|---|---|---|---|---|
| | 18 | 20 | 5 | 5 | 5 | | | 53 |
| Amount of treatment based on days in bed | 2 days | 3 days | 4 days | 5 days | 6 days | 7 days | 8–10 days | |
| | 12 | 10 | 7 | 21 | 1 | 1 | 1 | 53 |
| Failures—duration of pregnancy | 1–2 mos. | 3 mos. | 4 mos. | 5 mos. | 6–7 mos. | | | |
| | 3 | 2 | 2 | | 1 | | | 8 |
| Per cent carried successfully to viability | 85 | | | | | | | |

TABLE VI.—HABITUAL ABORTIONS—PRIVATE CASES

| Number of previous spontaneous abortions | 1 abortion | 2 abortions | 3 abortions | 4 abortions | 5 abortions | 6–10 abortions | over 10 | Total |
|---|---|---|---|---|---|---|---|---|
| | 15 | 25 | 5 | 2 | | 2 | 2 | 51 |
| Duration of pregnancy when treatment started | 1–2 mos. | 3 mos. | 4 mos. | 5 mos. | 6 mos. | | | |
| | 37 | 10 | 2 | 2 | | | | 51 |
| Number of 3 c.c. injections given | 5–9 ampuls | 10–19 ampuls | 20–29 ampuls | 30–49 ampuls | over 50 | | | |
| | | 8 | 5 | 10 | 28 | | | 51 |
| Failures based on amount of treatment | | 2 | | 1 | 1 | | | 4 |

cational Hospital patients for various reasons do not co-operate in a study of this kind as well as they might if they were a little higher in the economic and intellectual scale. No patient was admitted to these services unless definite evidence of threatened abortion was present, including a history of amenorrhea, bleeding, uterine contractions, and a positive Friedman test. To be considered successfully treated, the patient must have delivered a viable baby who left the hospital alive not under 7 days.

The routine of therapy instituted at Research and Educational Hospital and private practice consisted of injections of 3 cubic centimeters of aqueous corpus luteum extract every 4 hours for the cases of threatened abortion during the active bleeding or cramping period in addition to absolute bed rest. After symptoms of bleeding and pain subsided, patients were given 3 cubic centimeters daily for 5 to 7 days, and then 3 cubic centimeters twice a week until viability was reached. Home bed confined patients were given 12 cubic centimeters of aqueous corpus luteum extracts intravenously daily during cramping and bleeding period to reduce the number of house calls. Further treatment was as mentioned.

The habitual abortion group was treated by the injection intramuscularly of 3 cubic centimeters twice a week. Treatment was started as soon as diagnosis of habitual abortion was made. Patients who had previously spontaneously aborted were placed in this group. The group of patients consisting of placenta previa, premature detachment of the placenta and premature rupture of the membranes were treated in a similar manner to the threatened abortion cases.

In the management of obstetrical complications closely resembling abortion, such as premature onset of labor with or without the rupture of the membranes, it seemed likely that the use of aqueous corpus luteum extracts to inhibit uterine contractions might be valuable in retaining the fetus *in utero* at least until the age of viability. We have treated 8 patients with premature rupture of the membranes at various stages of pregnancy. We have been able to keep some of these women from going into labor for weeks or even months in a few cases. In such cases there is always the danger that the liquor amnii will become contaminated by the bacteria in the vagina and that these organisms will spread to the placenta and to the fetus. With the development of fever in such cases the uterus usually develops strong contractions which cannot be controlled by these injections. It would not be good judgment to prevent them

TABLE VII.—MISCELLANEOUS USES OF LUTEIN

| Conditions | Number of cases treated | Failures | Per cent terminating successfully |
|---|---|---|---|
| Premature separation of placenta | 46 | 4 | 91 |
| Placenta previa | 18 | 1 | 94.5 |
| Patients subjected to laparotomy during pregnancy | 29 | 0 | 100 |
| Premature rupture of membranes | 8 | 1 | 87 |

even if it were possible. Accordingly, as soon as such patients give any evidence of infection the corpus luteum extract injections are stopped and the uterus is encouraged to empty itself. Table VII shows the results of our treatment in these cases.

In the 46 cases of premature separation of the placenta, 26 had had bleeding upon more than one occasion before the pregnancy terminated successfully. Four patients had 4 periods of moderate bleeding, one of whom did not carry through to viability but delivered a 1050 gram baby that died 3 hours after delivery. Much the same was experienced in the placenta previa cases. In this series of 18 cases, 10 had more than 1 period of bleeding and 1 case had 4, before pregnancy terminated successfully by cesarean section—the baby weighed 1820 grams and left the hospital 3 weeks later weighing 2540 grams. In all the cases of premature separation of the placenta, old adherent clots were found on the placenta at the site of separation, and in those that were terminated by cesarean section, many old clots were found in the uterus.

In the cases of placenta previa, diagnosis was confirmed after delivery by finding the placenta over the cervical os during the cesarean section or in the cases that delivered vaginally by the marginal rupture of membranes and partial compression of the placenta. The average duration of time that the delivery of the baby was delayed was 36 days in both above series. The longest time that delivery was delayed was 57 days. These additional days *in utero* for the fetus meant the difference between a previable fetus and a viable fetus at the time of delivery.

In the series of 8 cases in which the membranes ruptured prematurely the delivery was delayed an average of 8⅝ weeks following the administration of aqueous corpus luteum extract. The longest time that labor was delayed was 5 months. This case threatened to abort three times during the 5 months. Each time abortion threatened the amount of aqueous corpus luteum extract given daily was increased until the symptoms of pain and bleeding subsided and then the dosage was reduced to maintenance. The patient delivered a 4½ pound baby at 8½ lunar months. The fetus was in no way deformed from the lack of cushioning effect of the amniotic fluid. The child at present is 2 years old and normal in every respect. Another labor was delayed 3½ months after the rupture of the membranes, 2 were delayed 8 weeks, one 6 weeks, one 5 weeks, and two 4 weeks. In all probability the added weeks *in utero* gave the fetus a definite advantage in surviving after delivery.

In the 29 cases upon which it was necessary to perform major surgery, no cases aborted. In this series there were 10 appendectomies, 9 operations for ovarian cysts, 5 myomectomies, and in 2 cases it was necessary to replace the uterus to its normal position following an interposition operation, done elsewhere, without sterilization. In 3 cases the abdomen was opened by mistake because the operator suspected fibroids whereas the uterus was found to be pregnant. It has been found to be advantageous to start the corpus luteum treatment as soon as surgery is contemplated and to continue after surgery. However, in emergency appendectomies results were excellent where it was necessary to give practically all treatment after operation.

Premature labor without rupture of the membranes occurs frequently and is often an unwelcome complication of pregnancy. Theoretically, it would seem to be due in most cases in which no obvious cause, such as a blow or fall is present, to a failure of the normal mechanism which prevents the uterus from yielding to the physiological impulse to empty itself of the foreign bodies in its cavity, the fetus, placenta and liquor. In the light of our present knowledge the most potent factor causing this inhibition is the corpus luteum hormones in the early weeks of pregnancy, and later a similar functioning hormone produced by the placenta. For this reason we have used injections of corpus luteum extracts to supplement the amount the patient is producing in her own ovary or placenta to inhibit the action of the labor or expulsion mechanism. There are various indications for the use of corpus luteum extracts in this connection. Primarily it should be used in patients with a nonviable live fetus *in utero*. In such cases it may be necessary to inject rather larger doses when active uterine contractions are present and to

cut down the number and size of the doses after the acute symptoms have subsided, thus a satisfactory maintenance dose is determined. Three cubic centimeters of aqueous corpus luteum extract three to five times a day at first, gradually decreasing to one 3 cubic centimeter ampul every other day or twice a week, depending on the activity of the uterus.

The material should be used prophylactically when operations on the uterus and adnexa become necessary during pregnancy, such as myomectomy, twisted ovarian cyst, incarcerated retroflexed gravid uterus, when necessity arises for a pregnant woman to take a long journey either by automobile, airplane, railroad or boat. For this purpose we usually advise 3 cubic centimeter ampuls, one twice a week and more often if necessary. If a patient has a psychic shock, such as bad news, extreme anger or fright, the administration of a few doses of the extract prophylactically is both logical and useful even before the symptoms of uterine contractions appear. In the same way it may be used prophylactically when intercurrent infections such as contagious diseases or pyelitis of pregnancy threaten to bring on uterine contractions because of the associated pyrexia. The injections may be used to combat the development of premature labor under these conditions or to prevent the onset of labor at or near term. The latter is much less likely to be successful than the former, and in either case it has been our experience that once real labor pains have started corpus luteum extract injections to stop them are useless. The danger of puerperal infection from uterine contamination under these circumstances is obvious.

### PLACENTA PREVIA

When the ovum is implanted and the placenta develops in the lower portion of the uterine cavity, it must inevitably detach in part with the formation of the lower uterine segment. The amount and suddenness of the detachment and the stage of gestation at the time the separation occurs determines in large measure the amount of bleeding and the danger to the life of mother and baby. The cause of the formation of the lower uterine segment is the painless contractions of the fundus of the uterus first described by Braxton Hicks, which gradually become stronger as term is approached. Unfortunately, the separation may be sufficient to give an alarming hemorrhage as early as the 26th to the 28th week. Under such circumstances even if the initial hemorrhage subsides without serious danger to the mother the decision to postpone delivery until viability of the baby requires considerable courage on the part of the patient and physician. Since no one can say when further separation may result from the continuance of the uterine contractions nor whether or not the resultant hemorrhage may prove fatal to both mother and baby, it becomes obvious therefore that a substance which can be relied upon to inhibit uterine contractions in a physiological manner should automatically stop the formation of the lower uterine segment, and thus stop placental separation and hemorrhage. Acting on this assumption, we have treated 18 cases of placenta previa in which it seemed desirable to permit gestation to continue for a few weeks longer to give the baby a better chance of survival. The results have been most gratifying. No serious secondary hemorrhage occurred during such treatment. Under these circumstances when the baby has attained sufficient intrauterine development, usually 32 weeks or more, we delivered it by cesarean section, or otherwise, depending on the conditions present in each case at the time it became necessary or advisable to terminate the pregnancy. This method has the advantage over all other procedures of eliminating vaginal manipulations of all kinds until time for delivery, thus decreasing the danger of puerperal infection after delivery.

### PARTIAL PREMATURE DETACHMENT OF THE PLACENTA

In a somewhat similar manner the injections of this hormone are used to quiet uterine contractions when the diagnosis of partial premature detachment of the placenta was made before the fetus has reached the age of viability. Under these circumstances the irritation produced by the presence of blood clots between the placenta and membranes at the site of placental detachment stimulate stronger Braxton-Hicks contractions which in turn

may cause more placental separation. The logical remedy therefore would seem to be to inhibit these contractions until the fetus has reached viability, and then to rescue it before further separation causes death by doing a cesarean section. This plan has been followed in 46 cases, with no maternal mortality, and a fetal mortality of 9 per cent. Since the maternal mortality has been quoted from 15 to 50 per cent by various writers, and the fetal mortality placed at from 50 to 100 per cent, it is obvious that this management is a distinct advance in the treatment of this condition. It may be objected that in these cases we are dealing with a minor degree of partial separation, and not the dangerous complete separation, and that therefore our results are not comparable with other reported series. The answer to this argument is that almost all complete separations go through the stage of partial separation, and that by prompt management of the incomplete variety, we obviate the more dangerous complete variety. Not a single case of this series went on to the formation of a Couvelaire uterus. It would appear then that when this serious pathological condition occurs in cases untreated by these injections, the failure to inhibit uterine contractions contributed to the uteroplacental apoplexy. When the hemorrhage was completely controlled by the injections, and when the evidence pointed to the fact that only a small amount of separation had occurred at the time the patient came under treatment, she was allowed to proceed with the pregnancy and to deliver spontaneously if no further hemorrhage occurred. However, the fetal heart tones were carefully and frequently observed for evidence of signs of embarrassment of the fetal circulation during the later weeks of pregnancy and during labor.

### EVALUATION OF STUDY

Since the early publication of favorable results in the treatment of threatened and habitual abortion by the use of corpus luteum extracts by Krohn, Falls, and Lackner, there has been considerable controversy regarding the efficacy of these injections. We have received reports indicating that the results obtained by following our line of treatment were excellent from certain men, and indifferent from others. Three factors at least may contribute to the production of these results.

It must be recognized that not all preparations contain the same amount of contraction inhibiting hormone or hormones, and not all patients have a living fetus *in utero* at the time they come to the physician for advice. The physicians using the corpus luteum extract often are not sure in their own mind of the efficacy of the material and therefore give it in a haphazard manner, or fail to impress the patient with the necessity of co-operating by carrying out orders strictly until all danger of delivering a nonviable premature fetus is past. Suffice it to say that more and more clinicians are convincing themselves of the clinical value by using the hormones instead of condemning their use on theoretical grounds.

The dosage necessary in a given case may be very difficult or impossible to estimate accurately. This is so because each woman is manufacturing her own hormones in the placenta, and the injections supplement this natural supply. We go on the general broad assumption that it is better to give too much rather than not enough. As soon as symptoms of abortion arise, therefore, large doses frequently employed intramuscularly or even intravenously are used until the symptoms are brought under control or until it is evident that the case cannot be controlled by the injections of corpus luteum extract. If the symptoms are controlled for 24 hours, the dose is gradually decreased and an attempt is made to determine a maintenance dose. This is continued until the viability of the baby is assured, about the 34th week.

The use of corpus luteum extracts in placenta previa and premature detachment of the placenta has raised considerable adverse criticism from some obstetricians. This according to their own statements is not based on the use of the hormone in this type of case, but on theoretical grounds entirely. Their objection is that one must not temporize with a dangerous condition like placenta previa since a fatal hemorrhage may follow any form of expectant treatment. We wish to emphasize that we do not advocate the use of hormone in all cases of this kind, or for an indefinite period of time in

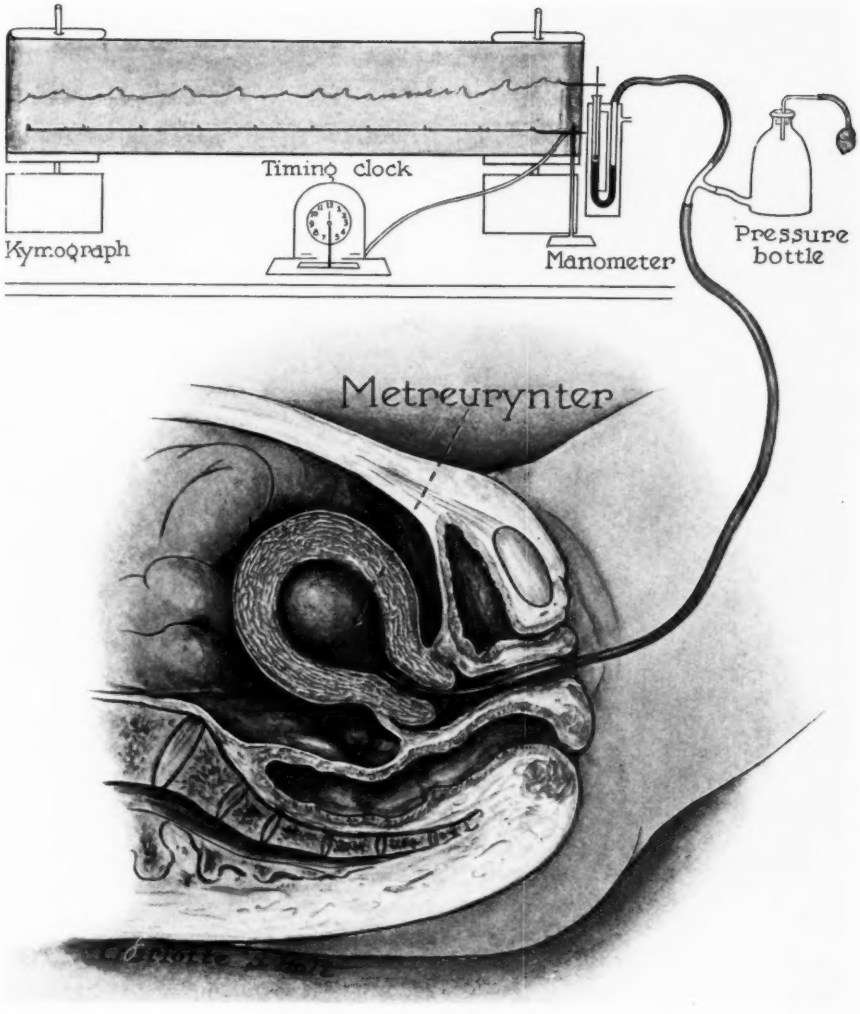


*Fig. 5. Method of demonstration (Moir).*
The metreurynter in 7 day puerperal uterus records contractions in response to stimulation by posterior pituitary extract producing kymographic tracings. Contractions are inhibited by subsequent injections of extracts of corpus luteum.

*Clinical and Experimental Observations on the Use of Corpus Luteum Extracts in Obstetrics.* —*Frederick H. Falls, George H. Rezek, and S. J. Benensohn.*

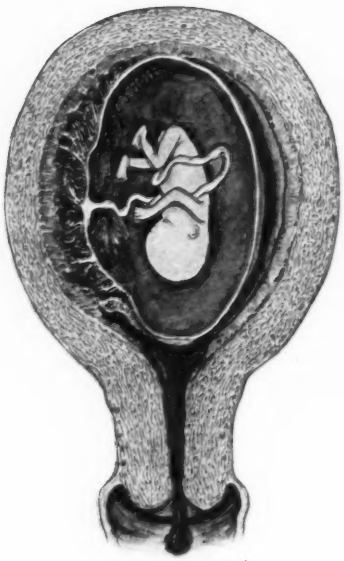

*Fig. 6. Threatened abortion*
*(3 month fetus).*
Injections reduce uterine irritability and prevent response to the stimulus producing abortion even after partial placental detachment.

*Fig. 7. Habitual abortion*
*(5 month fetus).*
Prophylactic injections started as soon as pregnancy is determined prevent uterine contractions which produce placental separation and fetal expulsion.

*Fig. 8. Premature rupture of membranes (7 month fetus).*

Usually results in expulsion of fetus within 24 hours. Injections often delay the onset of labor by days or weeks. They are contraindicated by evidence of infection.

*Fig. 9. Premature detachment of placenta (6 month fetus).*

Results in irritating intrauterine clots stimulating uterine contractions and further detachment. Injections stop contractions permitting development of nonviable fetus or, if viable, preparation for operation.

*Fig. 10. Premature onset of labor (8 month fetus).*

Weak pains of early premature labor are controlled by injections even after the partial dilatation of the cervix has taken place. After labor is well established, injections are useless.

*Fig. 11. Placenta previa (7 month fetus).*

Braxton-Hick contractions form lower uterine segment resulting in detachment and hemorrhage. Injections stop contractions and further separation, permitting fetus to develop to viability.

any case. We wish further to state that, in the presence of severe hemorrhage, hormonal treatment should be disregarded in favor of active measures to stop hemorrhage thus safeguarding the mother even at the sacrifice of a baby's life. If, on the other hand, a moderate hemorrhage occurs in a given case when the baby is almost viable, and stops spontaneously, or after injections of corpus luteum hormone, we are not forced to use radical measures. Now if we admit that further bleeding depends largely on uterine contractions directly or indirectly, and if it can be shown that these contractions can be stopped by the use of corpus luteum extract injections, we would not feel morally free of blame if either the mother or baby died under any other method of treatment, and we had failed to use the hormone. We are further fortified in this position because we have not as yet experienced the serious results by the use of the hormone so freely predicted by the men who have admittedly no experience in its use.

Whether the baby is alive or dead is an important consideration in many cases before treatment is started. It is usually easy to diagnose the intrauterine fetal death by the characteristic signs and symptoms. However, in certain instances the diagnosis may be much in doubt when the physical findings are difficult to make out. In these cases the Friedman modification of the Aschheim-Zondek test may help to determine whether or not pregnancy is present. Corpus luteum extracts may then be used while the uterus is kept under observation to see if normal development occurs. We have found that, if the fetus is dead, corpus luteum injections will not prevent its expulsion in most cases.

Among the various objections to the use of corpus luteum extracts in the treatment of abortion is the observation by Payne and others that in a considerable number of abortions there is evidence of abnormality of the fetus, the placenta, or both. The possibility therefore of preserving *in utero* a fetus that might become a monster or be deficient in some respect must have due consideration. The objection is theoretical and not real in our experience. We have delivered only one monster or deformed fetus in 650 cases, which would indicate that the occurrence in this case was in all probability accidental.

The use of the hormone when premature rupture of the membranes has occurred at or before the 32d week of gestation is both logical and desirable. Practically, it has been found to inhibit successfully the onset of labor in a large percentage of the cases. Under ordinary circumstances labor will start within 24 hours. We have found that the onset of labor pains can much more readily be prevented than stopped after they have started. Fever appearing a few hours after the membranes have ruptured is a contraindication to corpus luteum extract injections, since it usually means contamination of the amniotic sac from the vagina and often a certain degree of placentitis. The possibility of salvaging a living premature baby that would survive is naturally remote, and the sooner such a fetus is delivered the better for all concerned. We have had no case of serious puerperal sepsis or pelvic infection following the use of corpus luteum extracts in this type of case.

We have purposely avoided the use of sedatives and vitamin E preparations in treating these cases; not because we felt that the latter had no therapeutic value, but to prevent clouding the issue as to what was preventing the abortion. We wished to attribute the results obtained to one therapeutic agent only. In the light of reports concerning the favorable action of vitamin E therapy, especially on habitual abortion, it may well be that a combination of corpus luteum hormones and vitamin E therapy would be found to be more efficacious than either alone.

In no case was threatened abortion considered when patient simply spotted on a few occasions during pregnancy. In most instances the passage of clots or severe cramps gave evidence of active uterine contractions.

It is interesting and significant that the three independently conducted series here recorded provided almost indentical results.

Obviously, more investigation of the hormones of the corpus luteum is imperative to a better understanding of the results obtained by us and by other investigators. However, until such work has been completed we have shown that highly satisfactory results can be

obtained by the preparations at hand and at not too great expense not only in threatened and habitual abortion, but also in several other important obstetrical complications.

As a result of our observations of the frequency of abortion in pregnant women previously treated for sterility we used corpus luteum extract prophylactically in a series of private cases. The results seem to indicate that the hormone is of marked value in reducing the tendency to abortion in such cases. The hormone injections are made in the same manner as described for habitual abortion. In 45 cases 2 patients aborted. The abortion rate after the aqueous corpus luteum extract injections were used routinely was 5 per cent, whereas, previous to the use of the hormone 5 cases of this type miscarried in a series of 15.

It is difficult to determine the value of the corpus luteum injections in connection with many medical and surgical complications of pregnancy, such as pyelitis, pneumonia, appendicitis, twisted ovarian cyst, and fibroids of the uterus.

The danger of spontaneous abortion in connection with these diseases and surgical conditions is well known and generally admitted. Our combined experience leads us to believe that the use of corpus luteum extract prophylactically helps to prevent abortion or premature labor in well over 75 per cent of cases.

It may be well at this time to mention some of the unfavorable factors in the treatment of abortion by these injections. In private practice it may be difficult to get the necessary co-operation of the patient, after the acute symptoms have subsided. It may be difficult for the patient to be hospitalized and the physician cannot always make the regular visits, sometimes three a day which are necessary in order to maintain a pregnancy in a uterus threatening to abort. The expense involved often caused us to lessen the number of injections which should be given to reduce the pain and spotting. We have found that a visiting nurse often could be relied upon to give the injections.

The Cook County Hospital patients were on the whole less intelligent than the two other groups. Also as a group they entered the hospital at a later period of the abortion than other groups and therefore were not as favorable prospects from the standpoint of treatment.

The Research and Educational Hospital group were slightly more intelligent than the patients in Group II. They came under treatment slightly sooner in the course of the threatened abortion. However, the follow-up on these cases was much more difficult since they came from more widely scattered communities and inadequate social service and follow-up personnel was not available. The chief reason for failures in all groups were nonco-operation and undertreatment.

Syphilis as a serious cause of abortion in this series was very uncommon. In the 14 cases showing positive serological findings only 3 gave evidence that syphilis was a contributing factor.

For the purpose of this investigation, sedatives were not given to these patients except in the private practice of one of us (Dr. Rezek) because we wished to be able to say that the hormone only could be responsible for favorable results, and for the blame if they did not occur. However, we see no objection to giving mild sedatives to reduce irritability of the patient, except that the number and severity of cramp-like pains may serve as an index as to the necessity of increasing the dosage of corpus luteum extract.

## CONCLUSIONS

1. Corpus luteum extracts used in the series of 650 cases contain a substance which when injected intramuscularly or intravenously inhibit uterine contractions and thus help to prevent abortion.

2. The injections will not prevent abortion when the fetus is dead.

3. The injections are contraindicated in the presence of uterine infection or mole pregnancies.

4. The prolongation of gestation by means of these injections when the fetus is on the borderline of viability and premature delivery seems imminent is desirable and not unreasonably dangerous.

5. It has apparently proved efficacious in cases in which surgical emergencies necessi-

tated laparotomy in preventing the onset of labor and abortion.

6. Patients with fibroid uteri and sterility cases who eventually become pregnant should be given injections prophylactically until the fetus has reached viability.

7. No untoward results have been noted in those patients who received the aqueous preparations even when given in relatively large doses (15 c.c.) intravenously.

8. The success of the treatment described depends upon the regular administration of adequate dosage, and upon the continued cooperation of the patient under the close supervision of the physician.

## REFERENCES

1. ALLEN and DOISFY. Physiol. Rev., 1927, 7: 600–650.
2. BRAXTON-HICKS. Tr. Obst. Soc. London, 1872, 13: 216–231.
3. FALLS, LACKNER, and KROHN. J. Am. M. Ass., 1936, 106: 271–274.
4. KROHN, FALLS, and LACKNER. Am. J. Obst. & Gynec. 1935, 29: 198.
5. MOIR CLINIC. Brit. M. J., 1932, 1: 1022.
6. NOVAK and REYNOLDS. J. Am. M. Ass., 1932, 99: 1466.
7. PAYNE. Am. J. Obst. & Gynec., 1942, 43: 245–255.

# THE INTRAVENOUS USE OF AMINO ACIDS FOR NUTRITIONAL PURPOSES IN THE SURGICAL PATIENT

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THE value of a parenteral supply of protein to the patient who can not ingest, digest, or absorb food normally has long been appreciated. As early as 1902 attempts were made by Loewi to administer protein digests by mouth. Similar predigested meat products were given rectally by Abderhalden, and intravenously by Henriques and Andersen.

In 1934, Rose pointed out the possibility and advantages of maintaining a patient in nitrogen balance by administering a mixture of all the essential amino acids. However, the administration of such a mixture of pure isolated amino acids is prohibitively expensive, and in such a mixture the possibility exists that some essential amino acids may be lacking. In order to circumvent these difficulties, Van Slyke, and later Cox and Mueller worked with mixtures of amino acids derived from an acid hydrolysis of casein. It was then learned that this process destroyed the tryptophane, one of the essential amino acids. However, when the casein was hydrolyzed by slow enzymatic action, tryptophane was spared. This last preparation, when fed to rats orally, maintained nitrogen balance and produced the same gain in weight as did unaltered casein (10).

In 1939, Elman and Weiner (9) administered intravenously an acid hydrolysate of casein to which tryptophane and cystine were added. They found that nitrogen equilibrium could be maintained in humans with this mixture as the only source of protein. The following year, Elman (7) reported the successful intravenous administration of an enzymatic hydrolysate of casein to adults. Shohl, Butler, Blackfan, and MacLachlan reported similar work with children.

We wish to describe our experiences with an enzymatic hydrolyzed amino acid preparation, and shall consider: (1) a method of preparation; (2) intravenous dosage and toxic reactions; (3) evidence of utilization by the body; and (4) the effect on the regeneration of plasma proteins.

From the Surgical Service of Dr. Ralph Colp, and the Chemical Laboratory, The Mount Sinai Hospital, New York.

## PREPARATION

The enzymatic hydrolysate of casein, known as amigen, is supplied as a refined powder ready for use. It contains 12 per cent nitrogen, of which 26 per cent is polypeptide nitrogen, and the rest amino acid nitrogen. There is no unhydrolyzed protein. The ash content is 5.5 per cent and consists chiefly of sodium, chlorine, phosphorus, and sulphur (18).

The amigen is weighed out in 100 gram portions and each portion is dissolved in one liter of distilled water. The resulting 10 per cent solution is passed through a Berkefeld filter W and is diluted to a 5 per cent solution under sterile precautions. It is then sealed in a sterile container, steamed over a water bath for 30 minutes, and may be stored on ice or at room temperature.

There are a few simple precautions that deserve mention. If amigen powder is allowed to stand exposed to the air longer than a day, it absorbs moisture and turns into a firm, clay-like material which is difficult to dissolve. The powder should be dissolved within a few hours after a sealed container is opened. Inasmuch as amigen solutions are excellent culture media, strict asepsis must be maintained in preparation and administration. A solution which has been properly prepared for use should be clear, and subsequent clouding of the solution is a sign of contamination.

Glucose, thiamine chloride, nicotinic acid, ascorbic acid, and 0.8 per cent sulfanilamide solution may be added to amigen solution. However, the addition of sodium sulfapyridine and sodium sulfathiazole in 1 per cent solution produce precipitates that render the mixture unsatisfactory for intravenous use.

### INTRAVENOUS DOSAGE AND TOXIC REACTIONS

In calculating the dosage of amigen, one must remember that it is a food substitute, and therefore a number of factors should be taken into consideration; namely: (a) protein requirement, (b) previous state of nutrition, (c) other sources of food, (d) fluid balance.

The daily basal protein requirement for an adult is roughly 1 gram of protein per kilogram. Unpublished observations (18) have shown that 0.7 to 0.8 grams of amigen per kilogram per day will maintain an active man in positive nitrogen balance. Larger quantities of amigen are required if there are additional protein needs. This is necessitated by febrile states, and the formation of body exudates such as ascites. It is also indicated following extensive operative procedures in which there is an excessive nitrogen loss in the urine. This is probably due to local tissue destruction at the operative site and increased general protein utilization following temperature elevations.

The previous state of nutrition must also be considered in determining dosage. For example, if a state of chronic inanition has existed due to pyloric stenosis, obstructive lesion of the esophagus, or extensive ulcerative colitis, it is not only necessary to supply immediate protein needs, but it is vital to build up again depleted reserves.

If food may be administered via a gastrostomy or jejunostomy, or if the patient is able to take nourishment by mouth during the convalescent period, there is no further need for intravenous amino acids.

The state of the fluid balance plays a major rôle in limiting dosage. The use of amigen has been limited to 2½ to 5 per cent solutions because of toxic reactions which shall be discussed subsequently. Consequently it requires 1000 or 2000 cubic centimeters of fluid to administer 50 grams of amigen, depending upon the concentration. A 5 per cent glucose usually is added to the solutions to increase their caloric value. Since a combined 5 per cent glucose and 5 per cent amigen solution contains 400 calories, the basal caloric requirements are supplied by approximately 3 liters. This is not an excessive fluid intake unless the patient has hypoproteinemia, or cardiac or renal failure. If these conditions exist, with peripheral or pulmonary edema, the amount of amigen solution must be curtailed.

To summarize, it has been our practice to supply daily 50 to 100 grams of amigen in 2½ or 5 per cent solutions. To these are added sodium chloride, vitamins, and glucose in sufficient amounts to bring the caloric intake to 1200 to 2000 calories. The dosage is limited by fluid tolerance and certain toxic reactions.

Unfavorable reactions have been reported by others using intravenous amino acids. Shohl and associates found that in children, many developed febrile reactions and macular rashes. A small percentage of Elman's cases displayed chills and fever (7). Farr (11) describes the frequent occurrence of flushing, warm sensations, nausea and vomiting following the rapid administration of large quantities of amigen.

In this current series, amigen was given intravenously in doses of 50 to 100 grams to 75 patients. No manifestations such as urticaria, angioneurotic edema, or foreign protein febrile response have been observed.

In one group, 1000 cubic centimeters of a 5 per cent amigen solution was administered in 1½ hours. These patients frequently experienced flushing of the face, a feeling of warmth, and frontal headache. A few had retching and vomiting. None of these symptoms occurred when amigen was given slowly, i.e., 120 to 240 cubic centimeters per hour.

The one reaction that has caused concern is the development of phlebitis following the administration of hypertonic solutions. A 2½ per cent amigen solution is approximately isotonic (7), and is scarcely more irritating than normal saline. In fact, a 5 per cent amigen solution may be given continuously for 48 hours without causing phlebitis. Fortunately, no ill results were observed following an occasional infiltration of the perivenous tissues. The swelling which occurred disappeared completely without inflammatory reaction within 24 hours. However, if 5 to 10 per cent glucose is added so that the solution becomes markedly hypertonic, endophlebitis is liable to occur.

TABLE I.—AMINO ACID IN BLOOD AND URINE

| Case No. Name Number Date | Diagnosis | Blood | | | Interval | Urine | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Injection period Time a.m. | Amino acid nitrogen mgm. | Urea nitrogen mgm. | | Volume (quantity) c.c. | Amino acid nitrogen gms. per liter | Amino acid nitrogen total excreted gm. | Total nitrogen per liter gm. | Per cent Amino acid nitrogen |
| 1 J. P. 469427 2-26-41 | Post-operative appendicitis | 7:30 | 7.4 | 18 | 12:00– 7:00 p.m. a.m. | 300 | .15 | .045 | 14.3 | 1.0 |
| | | 8:30 | 7.0 | 20 | | | | | | |
| | | 9:00 | 9.2 | 22 | 7:00– 9:00 a.m. a.m. | 300 | .17 | .052 | 8.3 | 2.1 |
| | | 9:30 | 6.9 | 22 | | | | | | |
| | | 10:30 | 7.0 | 20 | 9:00–12:00 a.m. a.m. | 120 | .23 | .027 | 11.1 | 2.0 |
| | | 11:30 | 6.9 | 20 | | | | | | |
| 2 R.G. 469344 2-28-41 | Hernia | 7:30 | 7.0 | 20 | 12:00– 6:00 p.m. a.m. | 360 | .28 | .10 | 17.1 | 1.6 |
| | | 8:30 | 8.9 | 20 | | | | | | |
| | | 9:00 | 10.0 | 20 | 6:00–10:30 a.m. a.m. | 180 | .24 | .043 | 13.6 | 1.8 |
| | | 9:30 | 8.5 | 21 | | | | | | |
| | | 10:30 | 7.5 | 21 | 10:30–12:30 a.m. a.m. | 150 | .23 | .034 | 11.1 | 2.1 |
| | | 11:30 | 6.9 | 21 | | | | | | |
| 3 W.C. 468765 2-21-41 | Regional ileitis | 7:30 | 5.8 | 11 | 12:00– 6:00 p.m. a.m. | 180 | .078 | .014 | 9.8 | .8 |
| | | 8:30 | | | | | | | | |
| | | 9:00 | 8.8 | 12 | 6:00–10:45 a.m. a.m. | 300 | .33 | .099 | 8.7 | 3.8 |
| | | 9:30 | 8.9 | 13 | | | | | | |
| | | 10:30 | 6.6 | 14 | | | | | | |
| | | 11:30 | 4.8 | 15 | | | | | | |
| 4 H.H. 468543 3-2-41 | Duodenal ulcer | 7:30 | 6.5 | 14 | 12:00– 7:30 p.m. a.m. | 400 | .013 | .005 | 15. | .1 |
| | | 8:30 | 9.1 | 14 | | | | | | |
| | | 9:00 | 10.0 | 20 | 7:30– 9:30 a.m. a.m. | 150 | .28 | .042 | 15.4 | 1.8 |
| | | 9:30 | 8.3 | 20 | | | | | | |
| | | 10:30 | 6.6 | 19 | 9:30–11:30 a.m. a.m. | 120 | .15 | .018 | 14.3 | 1.1 |
| | | 11:30 | 6.2 | 11 | | | | | | |
| 5 A.K. 469544 3-10-41 | Duodenal ulcer with chronic nephritis | 7:30 | 6.4 | 30 | 12:00– 6:00 p.m. a.m. | 60 | .17 | .010 | 18.2 | .9 |
| | | 8:30 | 10.0 | 36 | | | | | | |
| | | 9:00 | 8.5 | | 6:00– 9:15 a.m. a.m. | 75 | .33 | .025 | 19.4 | 1.7 |
| | | 9:30 | 8.1 | 35 | | | | | | |
| | | 10:30 | 6.8 | 38 | 9:15–11:30 a.m. a.m. | 100 | .26 | .026 | 17.1 | 1.5 |
| | | 11:30 | 6.1 | 35 | | | | | | |
| 6 M.D. 469886 3-23-41 | Severe toxic hepatitis | 7:30 | 6.5 | 15 | 12:00– 7:30 p.m. a.m. | 400 | .11 | .043 | 4.3 | 2.5 |
| | | 8:30 | 8.7 | 16 | | | | | | |
| | | 9:00 | 10.1 | 21 | 7:30– 9:30 a.m. a.m. | 150 | .39 | .058 | 4.5 | 8.6 |
| | | 9:30 | 10.4 | 19 | | | | | | |
| | | 10:30 | 8.5 | 20 | 9:30–11:30 a.m. a.m. | 100 | .26 | .026 | 3.4 | 7.6 |
| | | 11:30 | 7.2 | 19 | | | | | | |

This danger of phlebitis may be minimized by inserting the needle at the junction of two veins, and administering the solution at a rate of only 2 to 4 cubic centimeters per minute. The hypertonic solution may thereby be more rapidly diluted with venous blood, and it becomes unnecessary to change the site of injection for at least 24 hours.

EVIDENCE OF UTILIZATION BY THE BODY

Two facts strongly support the theory that this amino acid mixture is utilized by the body for nutrition: (a) The amino acids are rapidly absorbed from the blood stream by the body tissues and are not lost in the urine. (b) A positive nitrogen balance may be maintained with amigen as the sole source of nitrogen.

*Absorption by the tissues.* Van Slyke and Meyer injected dogs with large amounts of an acid hydrolysate of casein and found that after a half hour, only 5 per cent remained in the circulation and 11 per cent was excreted in the urine. Elman (6) also reports similar results in dogs. Farr and MacFadyen (12) gave amigen to nephrotic children and found that the urinary loss was insignificant. Altshuler, Hensel, and Sahyun injected a 10 per cent solution of an acid hydrolysate of casein fortified with tryptophane and cystine into 8 normal persons. They found about a 10 per cent loss in the urine.

In order to study the absorption of amigen by the tissues and loss in the urine, a group of experiments was performed. Fifteen patients were selected. The diagnoses of this group are listed as follows: hernia, 4; duodenal ulcer, postoperative appendicitis, sciatic syndrome, hepatitis (2 mild, 1 severe), myasthenia gravis, muscular dystrophy, regional ileitis, duodenal ulcer with chronic nephritis, choledocholithiasis with jaundice.

Fifty grams of amigen in 1 liter of solution was administered to each patient. The time of injection was 1½ hours. Blood samples were taken at half hour intervals for a 4 hour period and tested for amino acid nitrogen and urea nitrogen. Urine collections were begun 8 hours prior to the injection period and were continued for several hours after. The urine was tested for amino acid nitrogen and total nonprotein nitrogen.

The amino acid nitrogen in the blood and urine was determined by the Folin colorimetric method, urea nitrogen by the Van Slyke aeration method, and the nonprotein nitrogen by the Nessler method (Table I).

As examples, the results of the tests in 6 patients are charted. The blood amino acids rose from fasting values of 5.8–7.4 milligrams per cent to a maximum of 10.4 milligrams per cent, and rapidly returned to normal. The amount of amino acid excreted in the urine never exceeded 0.6 grams which is equivalent to 1.5 per cent of the amino acids injected. The curves in all of the cases are very similar, with these two minor exceptions. The blood urea rose 8 milligrams per cent in Case 5, a patient who was in mild uremia. In the remainder, the blood urea showed only insignificant elevations. The other exception was in Case 6; a patient suffering from a moderately severe hepatitis in whom amino acid fraction of the total urinary nitrogen was as high as 8.6 per cent as compared to a normal of 1 to 2 per cent. We believe that these experiments warrant the conclusion that this preparation is rapidly absorbed from the blood stream by the body tissues and is not lost in the urine. This was noted in a variety of diseased states.

*Nitrogen balance.* The maintenance of positive nitrogen during the administration of amigen is evidence that the body utilizes this hydrolyzed protein. A number of authors have reported success in this regard in both laboratory animals and human subjects (4, 5, 7, 11, 15, 20, 24). Two cases, both in starvation, will be described briefly. Both attained positive nitrogen balance by means of intravenous amigen and glucose.

CASE 1. W.M. No. 472034. A white male was admitted April 19, 1941, to the service of Dr. John Garlock with a history of inability to swallow solid food for 5 weeks and liquids for 2 weeks. He had lost 35 pounds in weight. Physical examination revealed only marked malnutrition. X-ray and esophagoscopy demonstrated a carcinoma of the lower end of the esophagus. He was prepared for operation with the intravenous administration of amigen. Preoperative urinary nitrogen excretion promptly rose from starvation figures of an average of 4.3 grams per day, to normal levels, and positive nitrogen equilibrium was attained (Table II).

An intrathoracic esophagogastrostomy was then performed and a squamous cell carcinoma of the esophagus and an infiltrating adenocarcinoma of the cardiac end of the stomach were resected. The patient made a complete recovery. After operation, there was a huge nitrogen loss in the urine which was only partially replaced by the amino acids administered.

CASE 2. V. V., No. 471335. A 48 year old laborer was in excellent health until 5 months prior to admission, at which time he noted difficulty in swallowing and talking. He lost 30 pounds and was mark-

TABLE II.—CASE 1, W. M.

| Date | Nitrogen Intake | | Nitrogen Output | |
|---|---|---|---|---|
| | Amino acid nitrogen—gm. | Amino acids—gm. | 24 hour urine—c.c. | Total 24 hour urine nitrogen—gm. |
| 4–24 | | | 750 | 4.69 |
| 4–25 | | | 1300 | 4.10 |
| 4–26 | | | 1100 | 4.41 |
| 4–27 | 12 | 100 | 1500 | 9.00 |
| 4–28 | 12 | 100 | 1850 | 7.06 |
| 4–29 | 6 | 50 | 1250 | 8.25 |
| 4–30 | | | 1000 | 4.80* |
| 5–1 | | | 580 | 3.48 |
| 5–2 | | | 1800 | 15.64 |
| 5–3 | 9 | 75 | 600 | 7.35 |
| 5–4 | 9 | 75 | 1800 | 9.90 |
| 5–5 | 6 | 50 | 1600 | 6.10 |
| 5–6 | 6 | 50 | 2700 | 11.16 |
| 5–7 | 6 | 50 | 2370 | 0.12 |
| 5–8 | | | 2350 | 10.52 |
| 5–9 | | | 4000 | 13.04 |

*Operation.
Nitrogen balance is achieved temporarily in the starving patient by intravenous amino acids in the preoperative period. The large postoperative nitrogen loss is partly replaced by the same therapy.

edly emaciated. He was admitted to the service of Dr. I. Wechsler. On examination there was inability to swallow, labored breathing, diffuse wasting of musculature, especially the tongue. The diagnosis was amyotrophic lateral sclerosis. Stomach tube feedings were employed but were complicated by edema of the larynx and bronchopneumonia. Because of these difficulties, oral feedings were discontinued, and the patient was fed by the intravenous route, with 10 per cent glucose and 2½ per cent amino acids. Vitamins were added. After 2 weeks the patient began to run a spiking temperature and died of a bronchopneumonia and respiratory paralysis (Table III).

TABLE III.—CASE 2, V. V.

| Calories | Intravenous fluids—c.c. | Carbohydrates—gm. | Amino acid nitrogen—gm. | Total 24 hour urinary nitrogen—gm. |
|---|---|---|---|---|
| 1000 | 2200 | 200 | 6 | 3.1 |
| 1500 | 3300 | 300 | 7.5 | 7.8 |
| 1252 | 2750 | 250 | 7.5 | 9.9 |
| 2000 | 4400 | 400 | 12.0 | 7.5 |
| 1500 | 3300 | 300 | 9.0 | 7.1 |
| 1500 | 3300 | 300 | 9.0 | 7.9 |
| 1500 | 3550 | 300 | 9.0 | 8.4 |
| 1400 | 3600 | 300 | 9.0 | 10.6 |
| Total | | | 69.0 | 62.3 |

Nitrogen balance is achieved during an 8 day period by the intravenous administration of amino acids and glucose. Following this period bronchopneumonia and further progression of the disease resulted in death.

### THE EFFECT ON THE REGENERATION OF PLASMA PROTEINS

Theoretically one would expect that the administration of amino acids intravenously to patients with nutritional hypoproteinemia might supply the necessary basic factors for plasma protein regeneration. Whipple (17) has concluded from his experimental work that the tissue proteins were in "dynamic equilibrium" with those of the plasma. "Plasma protein is a part of a balanced system of body proteins; a steady state of ebb and flow exists between the plasma proteins and a portion of the cell and tissue body protein." It may be predicated, therefore, that if depleted tissue proteins are replenished by amino acids, an increase in plasma proteins would result. Clinical reports, however, have failed to show any startling rises in plasma protein following intravenous amino acid administration. Both Ravdin and Farr (11) have reported cases of hypoproteinemia which failed to respond to intravenous amino acid therapy. Two cases of hypoproteinemia are presented as examples, in which intravenous amino acid therapy was given.

CASE 3. A. B., Hospital No. 467788. A 57 year old furrier was admitted 25 years previously for pyloric stenosis, and a posterior gastroenterostomy was performed. Nine months ago he began to have 5 watery stools a day and fecal smelling eructations. He lost 40 pounds in weight. On examination he was cachectic. A gastrocolic fistula was demonstrated by x-ray. A preliminary right side spur colostomy was performed. Following this procedure the patient did poorly. Large amounts of fluids were lost by colostomy and the patient took very little by mouth. The blood protein fell to 4.3 grams per cent. He was given 475 grams of amigen in a space of 8 days, but the development of a phlebitis prevented further treatment. The gastrocolic fistula was disconnected, and a jejunostomy was established for feeding purposes. The patient made a complete recovery. (Table IV.)

CASE 4. H. K., Hospital No. 474685. A 59 year old housewife was admitted to the hospital as a private patient of Dr. S. S. Bernstein and Dr. John Garlock, complaining of postprandial nausea and

TABLE IV

| Date | Hematocrit | Plasma proteins gms./100 c.c. | Amino acids gm. |
|---|---|---|---|
| 3–25 | 35 | 4.2 | |
| 3–27 | | 4.4 | 50 |
| 3–28 | | | 50 |
| 3–29 | 40 | 5.0 | 50 |
| 3–30 | | | 50 |
| 3–31 | | | 50 |
| 4–1 | 36 | 4.6 | 100 |
| 4–2 | | | 50 |
| 4–3 | | 4.3 | 75 |
| 4–5 | 46 | *6.4 | |
| 4–8 | 39 | 5.8 | |
| 4–16 | | 5.4 | |

During a period of 8 days, patient received large amounts of amigen intravenously; oral feedings were limited. There was no elevation of plasma protein during the period of amigen injection.
*The elevation of plasma proteins following the amino acid therapy was related to hemoconcentration.

TABLE V.—CASE 4, H. K.

| Date | Hemoglobin | Plasma proteins gms./100 c.c. | Amino acids gm. |
|---|---|---|---|
| 7–7 | 88 | | |
| 7–8 | | 4.2 | 50 |
| 7–9 | 88 | | 50 |
| 7–10 | | 4.2 | 50 |
| 7–11 | 90 | | 50 |
| 7–12 | | 4.7 | 50 |
| 7–13 | 90 | | 50 |
| 7–14 | | | 50 |
| 7–15 | 90 | | 50 |
| 7–16 | | | 50 |
| 7–17 | 85 | | 50 |
| 7–18 | | | 50 |
| 7–19 | 80 | | 50 |
| 7–21 | 75 | 5.5 | |
| 7–23 | 71 | | |
| 7–25 | 71 | 4.8 | |
| 7–28 | 75 | | |
| 8–9 | | 5.1 | |
| 9–2 | | 5.1 | |

epigastric fullness of 3 months' duration. X-ray examination revealed an extensive carcinoma of the stomach. A total gastrectomy, esophagojejunostomy, and jejunojejunostomy were done. A jejunostomy for feeding was also performed.

The postoperative course was satisfactory for 1 week. By the 9th postoperative day, however, her abdomen became distended and pulse rapid and thready. Blood proteins fell to 4.2 grams per cent. Beginning on the 12th postoperative day, 600 grams of amigen were given in 12 days. The blood protein levels are given in Table V. Unfortunately, hematocrit determinations were not done, but some information as to hydration can be gained from the hemoglobin determinations which are recorded.

The patient also received transfusions and jejunostomy feedings in addition to amigen. Despite these measures the blood proteins remained low. Improvement was gradual and by the 9th week the patient left the hospital and was able to take a soft diet by mouth.

The above cases here briefly reported fail to show any significant elevation of the plasma proteins following intravenous amino acids. On the other hand no definite proof has been offered that amino acids given intravenously are valueless in cases of hypoproteinemia. These studies may be criticized from at least one standpoint; namely, that the amino acids were not given over a long enough period. This criticism is supported by studies of Madden and Whipple on the plasma protein regeneration. Following plasmapheresis in dogs, a readily available protein reserve was demonstrated which was sufficient to restore 40 to 60 per cent of the plasma proteins. When, however, both the reserve and plasma proteins have been depleted, and regeneration of these proteins occurs following the administration of exogenous protein, the reserve supply is replaced at least in part before the plasma proteins return to normal. A very similar process may have occurred in the 2 cases of hypoproteinemia here reported. The amigen administration may have produced some increase in the protein reserves that had been depleted by a long period of malnutrition. It is our opinion, nevertheless, that plasma or whole blood is unquestionably the ideal replacement in hypoproteinemia.

## INDICATIONS FOR AMINO ACID ADMINISTRATION

What, then, are the indications for the intravenous administration of amino acids? As Farr (10) has recently pointed out, the prime indication is starvation of a patient in whom it is impractical to give protein by way of the intestinal tract. When starvation is

accompanied by hypoproteinemia, plasma infusions should be given in addition to, but not in place of amino acids. The latter are needed for immediate nutrition and for building of protein reserves to prevent further plasma protein loss.

There is another reason for giving amino acids intravenously; namely, to prevent liver damage. Recently numerous investigations have demonstrated the value of a high protein diet in the protection of the liver (2, 8, 13, 19, 23). Since amigen is an effective protein substitute, it is logical to assume that it will function in the same way to protect the liver against damage. It might be advisable to use amino acids intravenously in treating hepatitis and prolonged obstructive jaundice.

## SUMMARY AND CONCLUSIONS

The preparation, dosage, and methods of intravenous administration of an enzymatic hydrolysate of casein are described. The toxic reactions are minimal and measures are suggested for their prevention. Evidence is presented that these amino acids are absorbed by the tissues and utilized in nutrition. The prime indication for administration is a starvation state, when a sufficient quantity of proteins cannot be made available through the gastrointestinal tract. This form of therapy is not an adequate substitute for plasma infusions in hypoproteinemia but should be used as a supplement to plasma.

## REFERENCES

1. Abderhalden, E., Franz, F., and Schittenhelm, A. Zschr. physiol. Chem., 1909, 63: 215.
2. Addis, T., Poo, L. J., and Leu, W. J. Biol. Chem., 1936, 115: 117.
3. Altshuler, S. S., Hensel, H. M., and Sahyun, M. Am. J. M. Sc., 1940, 200: 239.
4. Corbould, I., Clark, R. H., and McKechnie, R. E., Jr. Am. J. Digest. Dis., 1939, 6: 185.
5. Cox, W. M., Jr., and Mueller, A. J. Proc. Soc. Exp. Biol., N. Y., 1939, 42: 658.
6. Elman, R. Proc. Soc. Exp. Biol., N. Y., 1937, 37: 437.
7. Idem. Ann. Surg., 1940, 112: 594.
8. Elman, R., and Heifetz, C. J. J. Exp. M., 1941, 73: 417.
9. Elman, R., and Weiner, D. O. J. Am. M. Ass., 1939, 112: 796.
10. Farr, L. E. Connecticut M. J., 1941, 5: 24.
11. Idem. J. Pediat. 1940, 16: 679.
12. Farr, L. E., and MacFadyen, D. A. Proc. Soc. Exp. Biol., N. Y., 1939, 42: 444.
13. Goldschmidt, S., Vars, H. M., and Ravdin, I. S. J. Clin. Invest., 1939, 18: 277.
14. Henriques, V., and Andersen, A. C. Hoppe Seyler Zschr., 1913, 88: 357.
15. Hill, L. W. J. Am. M. Ass., 1941, 116: 2135.
16. Loewi, O. Arch. exp. Path., Lpz., 1902, 48: 303.
17. Madden, S. C., and Whipple, G. H. Physiol. Rev., 1940, 20: 194.
18. Mead Johnson & Co., Personal communication.
19. Messinger, W. J., and Hawkins, W. B. Am. J. M. Sc., 1940, 199: 216.
20. Mueller, A. J., Kemmerer, K. S., Cox, W. M., Jr., and Barnes, S. T. J. Biol. Chem., 1940, 134: 573.
21. Ravdin, I. S. Ann. Surg., 1940, 112: 576.
22. Rose, W. C. The Significance of the Amino Acids in Nutrition. The Harvey Lectures. Series XXX, 1934–35. P. 49–63. Baltimore: Williams & Wilkins Co., 1936.
23. Schifrin, A. Virchows Arch., 1932, 287: 175.
24. Shohl, A. T., Butler, A. M., Blackfan, K. D., and MacLachlan, E. J. Pediat., St. Louis, 1939, 15: 469.
25. Van Slyke, D. D., and Meyer, G. M. J. Biol. Chem., 1913, 16: 197.

# THE PRESENT STATUS OF VAGINAL HYSTERECTOMY

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REMOVAL of the uterus by the vaginal route must have been attempted by the earliest surgeons; that the surgeons of Alexandria performed the operation many years B.C. is quite probable. Among the Greek and Roman medical writings are allusions to the removal of the uterus through the vaginal route. However, the first case to be reported was by Berengaria (17) of Bologna in 1507 who performed a partial vaginal hysterectomy. During the next four hundred years methods for this operation were described by surgeons in several European countries. The first authentically reported vaginal hysterectomy in America was performed in 1829 by Warren who was professor of anatomy and surgery at Harvard. Between 1829 and 1877 a number of cases were reported, some highly successful and others less so, but no definite procedure was described or followed. It remained for Noeggerath of New York in 1877 to perform the first complete, definitely planned vaginal hysterectomy in America, and during the last quarter of the nineteenth century the operation gained popularity among a few American surgeons. Henrotin (17) has compiled a comprehensive historical review of the subject up to the beginning of the present century.

Individual methods have in recent years been described by Bissell, Pellanda, Werner, Gellhorn, Babcock, Heaney (14), Kennedy, Sampolinski, Chueco, and others. Older methods were in existence prior to the modifications introduced by these surgeons, each of whom has developed a more or less standard procedure, or has modified older and well known methods in an attempt to develop a superior technique. These are too numerous to describe separately, although most of the proposed procedures fall into two general groups: (1) those in which hemisection of the uterus is performed, and (2) those in which the uterus is removed intact following circumcision of the cervix. In any given case the selection of operative maneuvers will depend upon the skill of the surgeon, the disease present, the condition of the patient, and the state of the field of operation.

It is not the purpose of this paper to condemn abdominal hysterectomy, but to emphasize the value and scope of the vaginal method. In this country vaginal hysterectomy has never become widely popular, although as Babcock points out, it has been enthusiastically praised by the small group which has employed it extensively. Greater familiarity with the transabdominal approach to the pelvis appears to be the principal reason for the comparative popularity among surgeons of abdominal hysterectomy. As a consequence a subtotal hysterectomy is often performed when a total hysterectomy is advisable or preferable.

Heaney (14) in 1934 demonstrated how low the mortality and morbidity of this operation can be, and expressed the hope that it might find a place in the armamentarium of every gynecologist. Emmert believes the procedure to be relatively safe and states that the uterus can be removed by the vaginal route in over 80 per cent of all hysterectomies. Green-Armytage finds that, although the operation is not popular among British surgeons, there can be no question that it is accompanied by less shock, more rapid convalescence, and a lower mortality than is hysterectomy by the abdominal route. Danforth is convinced that this very valuable mode of treatment is being neglected and states that "as our skill increases we are inclined to use it more and more." Heaney, in discussing Danforth's paper, said: "I have done 831 vaginal hysterectomies in nonmalignant disease with three fatalities. Most of the operations were done for fibroids. Among these were 197 nulliparas, some with intact hymens. In the last 369 it was necessary to morcellate 93 times." Tyrone and Miller followed 170 cases in which vaginal hysterectomy had been performed and

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found that 96.5 per cent showed complete relief of the symptoms of which these patients had previously complained. Babcock says that vaginal hysterectomy is the "operation of choice if hysterectomy is required in the presence of hemorrhage and infection," and further says that the mortality in vaginal hysterectomy can be practically eliminated. Potter says, ". . . as my experience increases I am convinced there is no other operation in gynecology that can compare with it for results," and quotes Kennedy to the effect that in his practice the operation had a mortality of less than one-half that of the removal of the nonsuppurative appendix in America. Averett (1) points out that "a skillfully executed vaginal hysterectomy is a decidedly less formidable procedure as determined by its demonstrable effect upon the patient than is the same operation performed with equal skill by the abdominal route."

Despite numerous reports of a mortality rate of less than 1 per cent for vaginal hysterectomy, Miller finds that, with the average surgeon, the mortality from abdominal hysterectomy is never under 5 or 6 per cent and may run 8 to 10 per cent. Nevertheless, surgeons deliberately choose the more hazardous approach, apparently because they are fascinated by abdominal surgery, or because of a feeling that abdominal surgery confers greater distinction and substantially contributes to their recognition and reputation as abdominal surgeons.

During the past 30 years, my associates and I have performed 1,564 vaginal hysterectomies, in the first few years limiting the operation largely to cases of uterine prolapse and gradually extending its scope of usefulness (5). In the early years many vaginal hysterectomies were performed for carcinoma of the cervix and a few of these patients are still living, some after 15 years. X-ray and radium therapy is now the treatment of choice, and, except in a few instances, hysterectomy has been performed only after all evidence of malignancy was eliminated, or to cure a pyouterus after the use of radium.

In the period between January 1, 1925, and January 1, 1942, a series of 567 vaginal hysterectomies was performed by myself with 3 deaths, or a mortality of 0.53 per cent. During the past 4 years I have performed 307 vaginal hysterectomies without a death. In Table I the figures for a 7 year period are compared with those of the leading proponents of this procedure as compiled from the literature.

TABLE I.—MORTALITY

| Authors | Vaginal hysterectomy | | Abdominal hysterectomy | |
|---|---|---|---|---|
| | No. cases | Mortality | No. cases | Mortality |
| Heaney (15) | 627 | 0.47 | | |
| Emmert | 315 | 3.2 | | |
| Green-Armytage | 500 | 1.2 | | |
| Danforth | 266 | 0.0 | | |
| Tyrone | 311 | .64 | 137 | 2.2 |
| Babcock | 300 | 0.0 | | |
| Witherspoon* | 73 | 2.7 | 77 | 7.9 |
| Noble | 232 | .43 | | |
| Averett (2) | 934 | .33 | | |
| Smith | 363 | 0.0 | 93 | 0.0 |
| Blain | 567 | .53 | 89 | 2.67 |

*In the cases analyzed 15 surgeons performed the abdominal and 9 the vaginal hysterectomies.

## ADVANTAGES OF VAGINAL HYSTERECTOMY

The outstanding advantages of this procedure include the following:

1. Mortality and postoperative morbidity are lower. Shock practically never occurs.

2. Usually not more than 40 minutes is required for the operation, often including repair surgery of the pelvic floor.

3. Peritoneal viscera are not traumatized.

4. Since it is for the most part an extraperitoneal procedure, the danger of infection is decreased, and if infection is present, dependent drainage is provided.

5. Postoperative incisional hernia cannot develop, and there is no painful operative scar. The former is an important consideration in obese patients.

6. The infected cervix is always removed without peritoneal contamination. This precludes the persistence of a chronic focus of infection or the development of a carcinoma at the site of cervical erosion or ulceration.

7. The operation can be performed in conjunction with perineorrhaphy, repair of cysto-

cele, treatment of obstetric injuries, and other surgery without greatly increasing the time of operation or materially altering the condition of the patient.

8. The uterine adnexa may be removed if coincidental lesions are encountered.

9. The appendix may often be removed vaginally in addition to other surgery being performed.

10. Omental and intestinal adhesions to operative scars do not occur, and separation and infection of abdominal incisions are avoided.

11. The operation is well borne by the patient even in the face of a tedious morcellation of a large tumor mass.

12. As in abdominal hysterectomy, the field of operation may be extended in this procedure. If it is found impractical to continue the vaginal hysterectomy because of a former abdominal wall fixation operation or for any other technical reason, the operation may be completed by the abdominal route.

13. There is very little danger of damaging the bladder, ureters, or rectum. In our entire series we have injured the bladder or ureters in only one case. There was an escape of urine for 10 days following operation which did not prolong the patient's convalescence although it was a cause for worry.

14. The operation may be performed in elderly patients who are poor risks for abdominal surgery.

15. Vaginal hysterectomy can be performed in the presence of such general or complicating diseases as diabetes, cardiac disease, pulmonary tuberculosis, hypertension or nephritis, in any of which a laparotomy might be contraindicated, or in the very obese individual in whom laparotomy is hazardous.

16. The operation may be performed in the presence of old but still active parametritis which has not responded to conservative therapy, resorption of the chronic inflammatory infiltrate occurring after removal of the uterus.

17. Circulatory accidents such as embolism and thrombosis are largely avoided (Potter).

18. Pulmonary complications are fewer because the operation can usually be performed with nitrous oxide oxygen anesthesia and the Trendelenburg position need not be employed. The choice of an anesthetic is of little importance. Although we choose nitrous oxide oxygen in most instances, spinal, local or an intravenous anesthetic have at times been employed.

19. The cosmetic advantage of producing no abdominal scar is worthy of consideration.

### INDICATIONS FOR VAGINAL HYSTERECTOMY

The following diseases can be successfully treated by vaginal hysterectomy:

1. Benign neoplasm of the uterus. These tumors may be quite large and multiple, those extending above the umbilicus having been removed vaginally following morcellation.

2. Procidentia uteri. Vaginal hysterectomy was possibly first performed for complete descensus. Many of the present day writers, unacquainted with this field of surgery, consider prolapse the only indication for this procedure.

3. Extensive laceration, erosion, ectropion, and leucoplacia of the cervix. This type of lesion is frequently precancerous and should be eradicated when a hysterectomy is performed.

4. Functional bleeding, especially in the menopausal period, which does not respond to endocrine therapy (Ottinger; Heaney (16)).

5. Chronic subinvolution of the uterus.

6. Uterine polyps, especially those showing a tendency to recurrence or exhibiting early malignant changes (Ottinger).

7. Persistent uterine leucorrhea (Heaney).

8. Stenosis of the cervix which has not responded to less radical treatment, such as that following radium therapy producing pyouterus.

9. Chronic metritis (Green-Armytage).

10. Vaginal hysterectomy constitutes the most effective treatment for carcinoma of the corpus uteri. The uterus should be removed intact. Radium and x-ray therapy, while replacing surgery in carcinoma of the cervix, should be used only as an adjunct to surgery in carcinoma of the fundus. The use of radiation in younger women without proved malignant disease is less scientific and more radical than vaginal hysterectomy because of the destructive action of the rays on the ovaries.

### CONTRAINDICATIONS FOR THIS OPERATION

Opinions as to contraindications for vaginal hysterectomy depend largely upon the experience of the surgeon with the procedure and consequently his confidence in and enthusiasm for the method. It has been stated that the removal of particularly large uterine tumors should not be attempted vaginally and that vaginal hysterectomy should not be performed in the presence of pelvic inflammation, and in those cases in which pelvic surgery has been performed. However, large fibroids can be removed vaginally and chronic pelvic infection is not actually an obstacle. Extensive pelvic adhesions do not constitute a contraindication and can be dealt with as safely by the vaginal as by the abdominal route. Strictly speaking there is no definite contraindication, although there are certainly instances in which the transabdominal approach is preferable, and the decision as to method must be based upon the wisdom of the surgeon. Or, as stated before, there is no objection, should the vaginal approach be found impractical, to complete the operation by the abdominal route.

### TECHNIQUES OF VAGINAL HYSTERECTOMY

All of the varied procedures in vaginal hysterectomy fall into one of two groups; those in which the uterus is hemisected, as first described by Doyen, and those in which the uterus is removed intact. The former procedure is especially valuable when adnexal disease is present or a large tumor has to be delivered, the hemisection facilitating secondary operative maneuvers upon the attached adnexa. This method has been popularized in recent years by Werner. Because of the relative absence of vessels crossing the midline of the uterus, hemisection is followed by very little if any hemorrhage. The second type of operation in which circumcision of the cervix is followed by delivery of the intact uterus, is the usual procedure.

Different methods of handling the broad ligament and contained structures during delivery of the uterus are in use, such as the suture method and the clamp method (Price-Kennedy). In the latter method the clamps are left *in situ* for a number of days instead of reconstructing the pelvic floor by means of ligatures. Despite excellent results claimed for it by Kennedy, we believe the clamp method increases the possibility of injury to the bladder and ureters and can hardly be considered the best surgical procedure. Except in cases of prolapse much of the work is done blindly by the clamp method, and there is no more reason for performing a hysterectomy blindly by the vaginal than by the abdominal route.

The use of a ligature carrier and the taking of small bites of tissue as the operation proceeds, precludes the use of forceps or any equipment which would narrow the field of operation, obstruct vision, or complicate the procedure. The importance of careful hemostasis cannot be overemphasized here, where the operative field is small and should be well visualized. Elimination of clamps and forceps and the taking of small bites of tissue makes good hemostasis possible and renders injury to the bladder and ureters almost impossible. When excessive oozing is encountered, the tendency is controlled by the intramuscular administration of 10 to 40 milligrams of recrystallized oxalic acid solution (6).

While the technique of vaginal hysterectomy is varied to suit the various lesions for which it is performed, a typical procedure may be described as follows: With a weighted speculum in the vagina and a retractor in the anterior fornix lifting the anterior vaginal wall and the attached bladder well out of the way, the anterior lip of the cervix is grasped with a tenaculum. A circular incision through the vaginal mucosa is made at the periphery of the portio vaginalis of the cervix. Following circumcision of the cervix, the original incision is deepened, the vesicouterine ligament is cut, the vaginal mucosa is pushed up from the cervix, and the lower portions of the broad ligaments are encountered. The broad ligaments are then grasped in small bites with the ligature carrier, ligated, and severed. It will be found that this procedure can be carried on for some time before the cul-de-sacs are entered. The detached portions of the ligaments are pushed up and away to expose new tissues for ligation. As the operation proceeds the peritoneal folds and the anterior leaf of the anterior cul-de-sac come into view. If the operative

field is kept reasonably free of blood, there should be no difficulty in recognizing the various anatomical structures. When the peritoneum is entered the peritoneal leaf is secured by long catgut on forceps, which is then moved out of the operative field and the bladder elevated with a retractor before dealing with the remainder of the broad ligaments. This not only aids in visibility but eliminates the possibility of trauma to the bladder and, to a lesser degree, the ureters. As the posterior cul-de-sac is opened the peritoneum is sutured to the mucosa of the posterior fornix and held by a long suture with forceps attached. This exposes the ureterosacral ligaments, which are ligated, not *en masse,* but with rather small "bites." Ligation of these ligaments greatly increases the mobility of the uterus and enables it to be brought down so that the remainder of the broad ligaments and the round ligaments are easily secured by multiple ligatures, and cut. Thus the uterus is delivered intact. A temporary gauze pack is usually placed in the posterior cul-de-sac to prevent injury to the intestines. This is especially important if the uterus is to be bisected or, in the case of large tumors, morcellated.

If the uterus is large and it is decided to bisect it, the cervix is first amputated and the uterus is split. If this still does not provide enough room for operation, the uterus can be morcellated, starting at the midline and removing enough tissue to reduce it to more workable size. Often large fibroids can be removed intact, but sometimes they, too, have to be morcellated. In this event both sides of the bisected uterus are held apart by means of Lahey or vulsellum forceps while the operation proceeds. If the fundus has been completely bisected, one-half may be pushed into the abdomen while the other half is being dealt with, or one-half may be removed and a single Kocher hemostat temporarily applied, or both halves may be removed, and two Kocher forceps left in place while the suturing for hemostasis proceeds. After the uterus has been freed, adnexal tissue may be removed if this is found necessary. Following salpingectomy, or further surgical work upon the ovaries or tubes, the ligaments are sutured together. Before the wound is closed it is well to examine the appendix if it can be located in the right pelvis; an appendectomy, if decided upon, adds only a few more minutes to the operative time.

Any one of several closures can be made. The method of closure of the vaginal vault is also a matter of choice, three basic principles being kept in mind. The first is to maintain adequate support for the remaining pelvic organs and the vaginal vault by the proper approximation and suturing of the ligamentous structures of the pelvis during closure of the wound. The second is to peritonealize the raw surfaces, and the third is to maintain adequate drainage in all cases.

The pelvic floor is reconstructed by joining the round, broad, and uterosacral ligaments from either side with interrupted sutures. As the round ligaments are approximated, the anterior leaf of the anterior cul-de-sac is sutured to them in order to peritonealize the operative site completely. If the approximation sutures of the ligaments are allowed to remain long and are brought out as the vaginal mucosa is closed longitudinally by interrupted sutures, these are tied to the mucosal sutures. The mucosa will thus be tightly bound to the ligaments, thereby eliminating dead spaces and further oozing.

In the case of pelvic prolapse, the removal of the uterus is but a small part of the operation, and plastic procedures for the correction of cystocele, rectocele, or lacerated perineum must be completed. Gauze or a rubber or glass drainage tube should always be inserted. As a further precaution against bladder complications and as an aid to the comfort of the patient, a Foley catheter is placed in the bladder and allowed to remain for 3 to 5 days, at which time the pack is removed. If infection is present, sulfanilamide is packed into the operative wound before it is closed.

The preceding discussion of technique has obviously been quite general and emphasizes the pliability of this operative procedure and the fact that there should be no standard technique for vaginal hysterectomy. The technique should vary in the various situations for which it is indicated. The important point to emphasize is the grasping and ligating of the various structures as the operation proceeds, with care

not to include too large a piece of tissue in each "bite" because of the danger of the ligature slipping.

## OBSERVATIONS

While we advocate vaginal hysterectomy as the preferred method for removal of the uterus in the majority of cases, it must be realized that this is a major surgical procedure and its success, as well as that of other major surgery, depends upon the training and experience of the surgeon.

It is an operation for experienced surgeons and should logically be most properly and advantageously employed by one well trained in gynecological surgery. However, as in other surgical specialties, the general surgeon, as the result of special interest and experience, may become equally proficient. The younger surgeon would do well to select "easy" cases at first, extending the use of the operation as experience is acquired.

Quite naturally all treatment methods have enthusiastic adherents, which accounts for the fact that among those qualified to express an opinion, Potter advises the vaginal method in only 30 per cent of operations for the removal of the uterus, whereas Emmert believes that 80 per cent of hysterectomies can be performed vaginally. We believe that Emmert's estimate is a conservative one and are now performing nearly 90 per cent of hysterectomies by the vaginal route.

Greenhill is of the opinion that a hysterectomy constitutes excessive treatment for benign lesions of the cervix. With this view we are inclined to disagree, especially in the case of patients past the age of 40 years. The cervical portion of the uterus ordinarily measures between 3 and 6 centimeters in length. Infection of the cervix may extend almost the entire length of the cervical canal, usually farther than generally appreciated. Conization operations and amputation of the cervix are usually inadequate to eradicate the disease for which treatment is attempted. Coincident disease of the fundus and adnexa is too often present.

Its reproductive function once fulfilled, the uterus is a useless organ and not infrequently a distinct liability to the patient. To the woman over 40 years the loss of the uterus is not a serious matter. Vaginal hysterectomy by the experienced surgeon is but slightly more difficult than amputation of the cervix, possesses definite mechanical advantages and usually produces more satisfactory results.

Vaginal hysterectomy provides for the routine removal of the cervix which is too often not removed in abdominal hysterectomies. Failure to perform a complete hysterectomy is regrettable because, if for no other reason, more than 5 per cent of carcinomas of the cervix develop in the retained cervical stump left behind in a subtotal hysterectomy. Averett (1) states that about 20 per cent of women who had subtotal hysterectomies performed, who never have been pregnant, develop cervical stump cancer.

## CONCLUSIONS

1. It is believed that vaginal hysterectomy offers obvious advantages which are generally unrecognized.

2. The available procedures are such that they can be modified to meet practically any situation arising in the pelvis.

3. The operation carries a lower morbidity and mortality than does abdominal hysterectomy and can be performed in the presence of serious systemic complications.

4. There is no single standard technique for vaginal hysterectomy. We prefer the technique of grasping and tying small bites of tissue as the operation proceeds, eliminating forceps as far as possible, and believe it is the most practical technique in nearly all cases.

5. Postoperative complications of vaginal hysterectomy are rare, and if they occur, are of short duration.

6. Because of its several advantages this operation should be mastered and used by all surgeons doing pelvic surgery.

7. The conclusions drawn are based upon experience in performing over 1,500 hysterectomies by the vaginal route.

## REFERENCES

1. Averett, L. Am. J. Obst., 1938, 35: 978.
2. Idem. Pennsylvania M. J., 1939, 43: 136.
3. Babcock, W. W. Surg. Gyn. Obst., 1932, 54: 193.
4. Bissell, D. Tr. Am. Gyn. Soc., 1918, 43: 157.
5. Blain, A. W. Proc. Interst. Postgrad. M. Ass. N. America, 1935, October.

6. Idem. Arch. Surg., 1942, 44: 1117.
7. Chueco, A., Feldman, I., and Imaz, J. J. Bol. Soc. obst. gin. B. Aires, 1928, 7: 499.
8. Danforth, W. C. Am. J. Obst., 1938, 36: 787.
9. Doyen, E. Technique chirurgicale. Paris: Masson et Cie, 1897.
10. Emmert, F. J. South. M. J., 1939, 32: 715.
11. Gellhorn, G. Surg. Gyn. Obst., 1930, 51: 484.
12. Green-Armytage, V. B. J. Obst. Gyn. Brit. Empire 1939, 46: 848.
13. Greenhill, J. P. In Yearbook of Obstetrics and Gynecology. Chicago: Yearbook Publishers, 1940, p. 420, and 1941, p. 392.
14. Heaney, N. S. Am. J. Obst., 1934, 28: 751.
15. Idem. Am. J. Obst., 1935, 30: 269.
16. Idem. Am. J. Surg., 1940, 68: 284.
17. Henrotin, F. In Gynecology and Abdominal Surgery, Kelly, H. A. and Noble, C. P. Vol. 2, p. 759. Philadelphia: W. B. Saunders, 1910.
18. Hornung, R. Zschr. Geburtsh. u. Gyn., 1929, 96: 35.
19. Kennedy, J. W. Am. J. Surg., 1936, 33: 428.
20. Miller, J. C. J. Missouri M. Ass., 1932, 29: 347.
21. Noble, T. B. In discussion of Ottinger, R. C.
22. Noeggerath, E. N. York M. J., 1877, 25: 635.
23. Ottinger, R. C. Indiana M. Ass. J., 1935, 28: 20.
24. Pellanda, G. Lyon chir., 1929, 26: 50.
25. Potter, M. G. N. York State J. M., 1939, 39: 1962.
26. Sampolinski, A. Am. J. Surg., 1936, 32: 230.
27. Smith, P. H. Am. J. Obst., 1940, 40: 118.
28. Tyrone, C. H. Ann. Surg., 1938, 107, 836.
29. Warren, J. C. Am. J. M. Sc., 1829, 4: 536.
30. Werner, P. Surg. Gyn. & Obst., 1929, 49: 362.
31. Witherspoon, J. T., and Butler, V. Am. J. Surg., 1933, 22: 361.

# THE PROBLEM OF THE TREATMENT OF SECONDARY PEPTIC ULCER

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GASTROJEJUNAL ulceration remains a serious problem despite a trend to reserve operation on primary ulcers for those cases with bleeding, perforation, or obstruction. This is attested by the reported incidence of gastrojejunal ulcer, ranging from 1.7 to 24 per cent following gastroenterostomy and from 0.4 to 10 per cent following gastric resection (10). It was in the hope of clarifying the problem of treatment of secondary ulceration that the present study, based on 81 cases followed at the New York Hospital, was undertaken.

A review of the literature dealing with secondary ulcer reveals that, although much has been written on the subject, there is very little uniformity in either the substance of the reports or the manner of presentation. This is particularly unfortunate since the number of patients operated upon for secondary ulceration in any one clinic is not large enough to be of statistical value. For this reason it is suggested that reports dealing with the treatment of secondary ulcer be more or less standardized, and the following outline is submitted with this aim in mind (Table I).

## ETIOLOGY

Rather than review all the factors that have been said to be of importance in etiology, we shall summarize the conditions under which secondary ulcer is likely to develop.

First, these patients may be considered to be of a constitutional type—persons with so called ulcer diathesis—who under certain circumstances are predisposed to develop ulcer. The physiological make-up of these people direct psychic stimuli to the upper gastrointestinal tract, so that in the presence of other factors, ulcer may develop.

Second, the constant finding of considerable acid in the presence of gastrojejunal ulcer indicates that a relatively high acidity is important in the development, or in the persistence of, an ulcer. In this group of patients, all who were carefully studied had considerable amounts of acid (60 degrees or more of free hydrochloric acid with adequate volume). This must not be interpreted as conflicting with the well established facts that many people without ulcer have high acidity and also that many patients who are asymptomatic after gastroenterostomy likewise have high postoperative gastric acidity.

Third, and by no means least in importance, is the fact that there are exaggerated psychic stimuli which, in the presence of the preceding factors, play an important rôle in the development of ulcer. These psychic stimuli produce not only a more constant and greater amount of gastric secretion and abnormal motility but also a change in the vascularity of the stomach and duodenum; an ideal setting for ulcer formation.

Finally, a host of factors—poor operative technique, nonabsorbent sutures in the line of anastomosis, size and location of the stoma, irregular habits of living, overindulgence in alcohol and tobacco, faulty diet, etc.—have been considered as the cause of recurrent ulcer, but it is probably only in exceptional cases that one of these alone can be held primarily responsible.

These factors are emphasized because of their practical application in treatment. Since these patients have already proved their susceptibility to ulcer development, their prognosis should be guarded, no matter what form of therapy is instituted. Likewise, since all of the patients have considerable acid, surgical therapy should be directed toward reducing the acidity of the stomach. Finally, since 90 per cent were poorly adjusted to their environment, adequate treatment, whether conserva-

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TABLE I.—OPERATIVE PROCEDURES

| A. Operations for secondary ulcer | Total no. operations | Operative mortality | Follow-up results | | | Number followed |
|---|---|---|---|---|---|---|
| | | | Good | Poor | Died | |
| 1. Local procedures | | | | | | |
| Closure of perforated marginal ulcer after gastroenterostomy | 1 | 0 | | 1 | | 1 |
| after resection | 1 | 0 | | 1 | | 1 |
| Excision of marginal ulcer after gastroenterostomy | 3 | 0 | | 3 | | 3 |
| after resection | 1 | 0 | | 1 | | 1 |
| Ligation of bleeding point after gastroenterostomy | 1 | 1 | | | | 1 |
| after resection | | | | | | |
| 2. Pylorectomy after gastroenterostomy | 3 | 0 | 2 | 1 | | 3 |
| 3. Dismantling after gastroenterostomy for uncomplicated marginal ulcer | 11 | 0 | 2 | 9 | | 11 |
| for perforated marginal ulcer | 1 | 1 | | | | 1 |
| with local procedure on duodenum | 3 | 0 | 1 | 2 | | 3 |
| 4. Gastroenterostomy after closure of perforated ulcer | 7 | 0 | 2 | 5 | | 7 |
| after dismantling | 3 | 0 | | 3 | | 3 |
| after pyloroplasty | 2 | 0 | 1 | 1 | | 2 |
| 5. Gastric resection after closure of perforated ulcer | 7 | 0 | 5 | 2 | | 7 |
| after pyloroplasty | 1 | 0 | 1 | | | 1 |
| after dismantling | 4 | 0 | 4 | | | 4 |
| after gastroenterostomy | 10 | 1 | 5 | 2 | | 10 |
| after resection | 4 | 1 | 2 | 1 | | 4 |
| 6. Miscellaneous Exploratory laparotomy | 6 | 0 | 0 | 6 | | 6 |
| Excision of gastric ulcer after dismantling | 1 | 0 | 0 | 1 | | 1 |
| Resection of Roux in Y after dismantling | 1 | 0 | 0 | 1 | | 1 |
| B. Operations for gastrocolic fistula | | | | | | |
| 1. Excision of fistulous tract after gastroenterostomy | 1 | 0 | 0 | 1 | | 1 |
| after resection | | | | | | |
| 2. Dismantling | 7 | 2 | 1 | 2 | 2 | 7 |
| 3. Resection after dismantling of gastrocolic fistula | 2 | 1 | 1 | | | 2 |
| after posterior gastroenterostomy | 1 | 0 | 1 | 0 | | 1 |
| after resection | | | | | | |
| 4. Preliminary cecostomy followed by one of above | | | | | | |

NOTE:
At first glance this outline may seem much too complicated, but even this detailed outline fails to cover all possibilities.

tive or operative, must include a proper mental adjustment of the patient. However, in emphasizing these factors it is not meant that sound surgery is to be forced into the background but rather that these factors should be constantly borne in mind in planning operative therapy.

## TREATMENT

Treatment of these ulcers may either be conservative or operative, except for those complicated by free perforation or gastrocolic fistula, both of which demand operation. Perforation into the free peritoneal cavity while rare, demands immediate operation, and the

TABLE II.—RESULTS IN GASTROCOLIC FISTULA BY ANY RECONSTRUCTIVE PROCEDURE

| Author | No. cases | Deaths | Results | | |
|---|---|---|---|---|---|
| | | | No. followed | Good | Poor |
| Allen | 8 | 2 | | | |
| Benedict | 5 | 1 | 3 | 2 | 1 |
| Finsterer | 19 | 7 | | | |
| Lahey and Swinton | 8 | 5 | | | |
| Pfeiffer | 3 | 0 | 3 | 2 | 1 |
| Rife | 10 | 2 | 8 | 6 | 2 |
| von Haberer | 20 | 4 | | | |
| Walter and Claggett | 50 | 16 | | | |
| Wright | 46 | 12 | 26 | 13 | 13 |
| New York Hospital | 8 | 3 | 5 | 3 | 2 |
| Total | 177 | 52 | 45 | 26 | 19 |
| Per cent | | 30 | | 58 | 42 |

simplest procedure—plication of the ulcer—is indicated. Occasionally, however, the ulcer may safely be resected with a revision of the stoma, but only in those patients whose condition is good and in whom the perforation is recent. Unlike simple ulcers, the secondary ulcers that perforate are rarely cured, and if symptoms persist after recovery from operation, gastric resection should be done without hesitation.

Gastrocolic fistula—a most serious complication of marginal ulcer—also demands operation, but not until adequate therapy including blood transfusions and vitamins has been administered. Patients suffering from this condition usually are poorly nourished, frequently anemic, and sometimes show evidence of avitaminosis—all potential contributors to a high operative mortality (Table II). Preliminary cecostomy has been advocated as an important aid in the preoperative preparation of these patients for the major operation and it has proved very satisfactory in the small group reported by Pfeiffer. As to operative treatment, both the poor condition of the patient and the technical difficulties make the simplest procedure, once again, the most advisable. In most cases this is dismantling of the gastroenterostomy with closure of the fistula. Strangely enough, although the original ulcer may be completely healed at the time of dismantling, it soon recurs. In this event resection should be done at an early date since severe hemorrhage is not uncommon. Occasionally a gastric resection may be done at the time of the original dismantling procedure, but this must be reserved for the few patients who are in excellent physical condition. Various methods of handling the large bowel have been suggested, but primary closure should be the procedure of choice.

### HEMORRHAGE

Hemorrhage—the most frequent complication of marginal ulcer—is fortunately not often severe enough to warrant immediate operation. Most patients respond to conservative therapy and, if bleeding is the first and only symptom, a medical regimen should be employed in an attempt to allow the ulcer to heal. However, if the response is unsatisfactory, gastric resection should be done. Occasionally immediate operation is necessary because of the continuation of bleeding for over 48 hours even after adequate conservative therapy has been instituted. In such case, a direct attack on the bleeding point must be made and, because the bleeding is frequently from a jejunal ulcer, a dismantling may be required to control the hemorrhage. If the primary operation has been a gastric resection, the bleeding marginal ulcer should be excised and a revision of the stoma performed. Sometimes this is not feasible and secondary resection must be done, but, since the latter is attended by a high mortality rate it should, if possible, be avoided.

It has been our observation that when bleeding occurs in a patient who has had a gastroenterostomy for a duodenal ulcer, the hemorrhage in most cases originates from a marginal or jejunal ulcer rather than from a persisting (or recurrent) duodenal ulcer (6). Failure to realize this fact has in some cases led to erroneous diagnoses and hence to improper operative treatment. Frequently the active ulcer is not demonstrable by x-ray; and often at operation, especially after a short period of supportive therapy has elapsed, the acute marginal ulcer cannot be recognized. It is, however, fallacious to assume that such an ulcer did not exist at the time of hemorrhage. We,

TABLE III.—LOCAL PROCEDURES—EXCISION OF ULCER, ENLARGEMENT OR REVISION OF STOMA

| Author | No. cases | Deaths | Results | | |
|---|---|---|---|---|---|
| | | | No. followed | Good | Poor |
| Alessandri | 16 | 2 | | | |
| Benedict | 5 | 1 | 3 | 0 | 3 |
| Starlinger | 2 | 1 | 1 | 0 | 1 |
| Walter and Claggett | 4 | 1 | 3 | 1 | 2 |
| Wright | 64 | 4 | 41 | 9 | 32 |
| Zukschwerdt and Eck | 4 | 1 | | | |
| New York Hospital | 3 | 0 | 3 | 0 | 3 |
| Total | 98 | 10 | 51 | 11 | 40 |
| Per cent | | 10 | | 22 | 78 |

TABLE IV.—DISMANTLING OF GASTROENTEROSTOMY

| Author | No. cases | Deaths | Results | | |
|---|---|---|---|---|---|
| | | | No. followed | Good | Poor |
| Alessandri | 5 | 0 | 5 | 0 | 5 |
| Benedict | 6 | 1 | 5 | 1 | 4 |
| von Haberer | 4 | 0 | 2 | 2 | 0 |
| Walter and Claggett | 93 | 9 | 70 | 18 | 52 |
| Wright | 106 | 11 | 61 | 23 | 38 |
| New York Hospital | 14 | 0 | 14 | 3 | 11 |
| Total | 228 | 21 | 157 | 47 | 110 |
| Per cent | | 10 | | 30 | 70 |

therefore, believe that in an elective secondary operation for repeated bleeding, the operation of choice is dismantling and gastric resection of the Pólya type, rather than a simple pylorectomy.

### UNCOMPLICATED MARGINAL ULCER

The present treatment of uncomplicated secondary ulcer is, in general, far from satisfactory. Conservative therapy is held by most surgeons to be unsuccessful chiefly because of the high incidence of such complications as hemorrhage, perforation and gastrocolic fistula; some (16) have even concluded that every patient with a proved marginal ulcer should be subjected to operation. This policy, however, is probably too extreme, for undoubtedly a few secondary ulcers will heal satisfactorily under conservative therapy. Hurst, for example, reports that in a group of 25 patients such therapy cured 50 per cent, a much better result than was obtained in the patients in our group treated in this manner. In our group of 51 patients the results of conservative treatment were good in 11, or 21 per cent, poor in 35, or 69 per cent, and 5 patients, 10 per cent, died. Of the 35 poor results, 23 patients were subsequently operated upon for persistent symptoms. Benedict, and Lahey and Swinton in smaller series of cases, report results similar to those of Hurst.

To be successful, however, medical therapy should include not only an initial period of rest in bed, a restricted diet, and abstinence from tobacco and alcohol, but also, and most important, a readjustment of mental attitude and adequate accommodation of the patient to his environment. The importance of the latter cannot be overemphasized; and it is interesting to find that, among the patients treated conservatively in our series, 9 of the 11 who responded satisfactorily were able in some way to make satisfactory mental adjustments. On the other hand, 29 of the 35 patients who failed to respond, also failed to adjust themselves satisfactorily. These figures accentuate the necessity for adequate psychiatric instruction as a major constituent of adequate conservative therapy. In general, a reasonable conclusion from the present evidence would seem to be that, if a really complete regimen of medical therapy is available, it should be given a trial but, if within a short time the ulcer has not healed, operation should be advised.

Satisfactory operative treatment up to the present time has been better achieved when gastric resection was done. This is particularly true in the treatment of marginal ulcer following gastroenterostomy. Local procedures, such as excision of the ulcer and enlargement or revision of the stoma, usually prove unsatisfactory and only delay the indications for more radical operation (Table III). One operation that has been widely used is a dismantling of the gastroenterostomy and restoration of the normal continuity of the gastrointestinal tract. This procedure has been found to be unsatisfactory, for, although

TABLE V.—GASTRIC RESECTION FOR MARGINAL ULCER AFTER GASTROENTEROSTOMY

| Author | No. cases | Deaths | Results | | |
|---|---|---|---|---|---|
| | | | No. followed | Good | Poor |
| Alessandri | 52 | 8 | | 39 | 5 |
| Benedict | 6 | 0 | 6 | 4 | 2 |
| Finsterer | 148 | 13 | 96 | 88 | 8 |
| Starlinger | 27 | 6 | 17 | 11 | 6 |
| Walter and Claggett | 52 | 4 | 45 | 32 | 13 |
| Wright | 166 | 29 | 108 | 82 | 26 |
| Zukschwerdt and Eck | 41 | 8 | | | |
| New York Hospital | 14 | 1 | 14 | 11 | 3 |
| Total | 506 | 69 | 329 | 267 | 62 |
| Per cent | | 13 | | 81 | 19 |

the marginal ulcer is cured, the conditions which led to the formation of the primary ulcer have not been altered, and these result in a 65 per cent recurrence of the original ulcer (Table IV). In an effort to avoid this, dismantling has been supplemented by some type of plastic procedure at the site of the original ulcer. Unfortunately, these results also have been disappointing.

Because of the inadequacy of the less radical procedures, gastric resection has long been used, although not uniformly accepted, as the operation of choice in the treatment of secondary ulceration, and the results obtained are uniformly better than those following any other surgical procedure (Table V). The largest series are reported by German authors (5, 8), who state that 90 per cent of the patients had good results. Finsterer makes an important distinction between the operative mortality rates of resection following different original procedures and reports a mortality rate for resection of 8.1 per cent after a previous gastroenterostomy in contrast to one of 23 per cent following a previous resection.

The problem of secondary ulcer after a resection is a much more serious one, since surgical therapy is limited to either a more extensive resection or an excision of the ulcer with revision of the stoma. Because the latter generally fails to prevent another recurrence, resection is strongly advised if circumstances permit; but the exceedingly high mortality of 20 to 25 per cent in secondary resection should be borne in mind while therapy is being planned. Since recurrences do take place and the mortality is not low, resection should not be regarded as infallible or be undertaken lightly and for these patients in particular, conservative therapy should be given a fair trial.

The problem of the recurrence of a primary ulcer, either after suture of a perforation or pyloroplasty or excision, is a relatively simple one. It is generally agreed that, if surgery is to be done, resection is the procedure of choice since less radical methods result in such a high percentage of failures.

Finally, whatever the operation that is undertaken, it should be planned so that it can be terminated at any time. For instance, if a gastric resection has been decided upon, the gastroenterostomy should first be dismantled and then, if the condition of the patient permits, the resection can be completed. In this manner the operative mortality can be kept at a minimum.

## CASE STUDIES

Material for this investigation was assembled from 81 patients, 28 of whom after their original operation were treated conservatively and 53 of whom were subjected to secondary operative treatment. In this latter group of 53 patients there were 135 operations (53 primary and 82 secondary) for ulcer or its complications—an average of 2.5 operations per patient (Table VI). Every patient originally had a gastric or duodenal ulcer except one who was found to have both a gastric ulcer and a leiomyoma of the stomach. Although all the patients had their reconstruction operations in this hospital, 35 had their original operative procedures elsewhere. In every case there has been a careful follow-up study so that each patient has been seen at regular intervals of not more than 1 year. Thus, in the computation of final results our conclusions are derived from several examinations, in addition to which x-ray studies were usually available. Since the results are based primarily upon subjective findings, they have been classified as either good or poor rather than as recurrent or cured. On the whole we

TABLE VI.—CASE REPORTS*

| Name Age in years | Duration of symptoms | No. | Procedure | Date | Lesion | Result |
|---|---|---|---|---|---|---|
| T. 20 | 6 yrs. | 1 | PGE | 1919 | DU | Poor |
| | 2 yrs. | 2 | Dismantling | 1933 | MU | Poor |
| M. 45 | 25 yrs. | 1 | PGE | 1928 | DU | Poor |
| | 5 yrs. | 2 | Excision of MU and revision of PGE | 1936 | MU | Poor |
| S. 48 | 15 yrs. | 1 | PGE | 1926 | GU | Poor |
| | 7 yrs. | 2 | Dismantling | 1933 | MU | Good |
| C. 43 | 8 yrs. | 1 | Pyloric exclusion and PGE | 1927 | DU | Poor |
| | 1½ yrs. | 2 | Laparotomy | 1929 | Adhesion | Poor |
| | 1½ yrs. | 3 | Gastrotomy | 1931 | Adhesion | Poor |
| | 2 yrs. | 4 | Excision of MU and revision of PGE | 1933 | MU | Poor |
| | 6 yrs. | 5 | Pólya resection | 1939 | MU | Poor |
| T. 47 | 2 yrs. | 1 | PGE | 1927 | MU | Poor |
| | 5 yrs. | 2 | Dismantling and excision of GU | 1937 | GU and MU | Poor |
| B. 51 | 2 yrs. | 1 | PGE | 1924 | DU | Poor |
| | 5 yrs. | 2 | Dismantling and excision of GU | 1937 | GU and MU | Poor |
| C. 40 | 6 yrs. | 1 | PGE | 1938 | DU | Poor |
| | 6 wks. | 2 | Anterior Pólya | 1939 | MU | Good |
| G. 35 | 1 yr. | 1 | PGE | 1919 | DU | Poor |
| | 15 yrs. | 2 | Dismantling of MU | 1935 | MU | Poor |
| | 1 yr. | 3 | Anterior PGE | 1936 | DU | Poor |
| | 3 mos. | 4 | Pólya resection | 1937 | MU | Poor |
| | 8 mos. | 5 | Secondary Pólya | 1938 | MU | Died (p.o.) |
| G. A. 48 | 10 yrs. | 1 | Billroth II | 1932 | DU | Poor |
| | 4½ yrs. | 2 | Excision of MU; revision, Roux anastomosis | 1937 | MU | Poor |
| | 1 yr. | 3 | Pólya | 1938 | MU | Good |
| F. 39 | 10 yrs. | 1 | PGE | 1936 | DU | Poor |
| | 2½ mos. | 2 | Exploratory laparotomy | 1939 | Adhesion | Poor |
| | 3 wks. | 3 | Pólya | 1940 | MU | Good |
| S. 36 | 3 yrs. | 1 | PGE | 1935 | DU | Poor |
| | 5 mos. | 2 | Dismantling and pyloroplasty | 1936 | MU | Poor |
| | 2 mos. | 3 | Pólya resection | 1937 | DU | Good |
| A. 29 | 9 yrs. | 1 | PGE | 1927 | DU | Poor |
| | 6 yrs. | 2 | Closure perforation of MU | 1938 | MU | Poor |
| | 1 yr. | 3 | Dismantling | 1939 | MU | Poor |
| | 2½ wks. | 4 | Resection with exclusion | 1940 | DU | Good |
| P. 46 | 10 yrs. | 1 | Suture of perforated ulcer | 1933 | Perf. DU | Poor |
| | 3 mos. | 2 | PGE | 1934 | DU | Poor |
| | 2 yrs. | 3 | Pólya resection | 1940 | MU | Poor |
| S. 26 | 5 mos. | 1 | Resection Pólya | 1926 | DU | Poor |
| | 2 mos. | 2 | Excision of MU | 1929 | MU | Poor |
| | 8 hrs. | 3 | PGE | 1934 | Perforating MU | Poor |
| S. 34 | 2 yrs. | 1 | PGE | 1934 | DU | Poor |
| | 3 mos. | 2 | Exploratory laparotomy | 1934 | JU | Poor |
| | 5 days | 3 | Gastrotomy, ligation of bleeder | 1934 | JU | Died (p.o.) |

PGE, posterior gastroenterostomy; MU, marginal ulcer; GU, gastric ulcer; DU, duodenal ulcer; GCF, gastrocolic fistula.

TABLE VI.—CASE REPORTS*—Continued

| Name Age in years | Duration of symptoms | No. | Procedure | Date | Lesion | Result |
|---|---|---|---|---|---|---|
| B. 40 | 10 yrs. | 1 | PGE | 1938 | DU | Poor |
| | 10 mos. | 2 | Resection | 1939 | MU | Poor |
| S. 41 | 9 yrs. | 1 | PGE; excision of GU and tumor, benign | 1934 | GU and benign tumor | Poor |
| | 1 day | 2 | Exploratory laparotomy. Gastrotomy | 1939 | GU | Died (p.o.) |
| B. 34 | 1½ yrs. | 1 | PGE | 1923 | DU | Poor |
| | 1 yr. | 2 | Dismantling | 1936 | MU | Poor |
| | 2 wks. | 3 | Gastric resection, Billroth II | 1937 | DU | Good |
| C. 24 | 1 yr. | 1 | PGE | 1916 | DU | Poor |
| | 3 yrs. | 2 | Dismantling | 1934 | MU | Poor |
| | 3 yrs. | 3 | Pyloric exclusion and anterior GE | 1937 | DU | Poor |
| | 3 yrs. | 4 | Gastric resection | 1940 | MU | Good |
| W. 43 | 3 yrs. | 1 | Plication of perforated DU and PGE | 1924 | Perforated DU | Poor |
| | | 2 | Plication of perforated MU. Dismantling | 1932 | Perforated MU | Died (p.o.) |
| M. 27 | 6 yrs. | 1 | PGE | 1931 | DU | Poor |
| | 3 yrs. | 2 | Revision of PGE, enlargement | 1935 | Stenosis | Good |
| S. 50 | 1 yr. | 1 | PGE | 1920 | GU | Poor |
| | 15 mos. | 2 | Dismantling | 1922 | MU | Poor |
| | 2 yrs. | 3 | Excision of GU | 1932 | GU | Poor |
| S. 34 | 10 yrs. | 1 | Subtotal gastrectomy | 1931 | DU | Poor |
| | 1 yr. | 2 | Pólya resection | 1939 | MU | Good |
| M. 38 | 6 yrs. | 1 | PGE | 1936 | DU | Poor |
| | 3 mos. | 2 | Pólya resection | 1940 | MU | Good |
| O. 26 | 4 days | 1 | Plication of perforated ulcer and PGE | 1932 | Perforated DU | Poor |
| | 5 yrs. | 2 | Dismantling | 1939 | MU | Good |
| B. 24 | 2 yrs. | 1 | Suture perforated ulcer | 1926 | Perforated DU | Poor |
| | 8 wks. | 2 | PGE | 1934 | DU | Poor |
| | 6 yrs. | 3 | Pylorectomy | 1940 | DU and MU | Poor |
| | 2 mos. | 4 | Gastric resection | 1940 | MU | Good |
| S. 33 | 6 yrs. | 1 | PGE and appendectomy | 1924 | DU | Poor |
| | 3 yrs. | 2 | Dismantling gastrocolic fistula; Finney pyloroplasty | 1938 | GCF | Died (p.o.) |
| B. 63 | 3 yrs. | 1 | PGE | 1933 | DU | Poor |
| | 1½ yrs. | 2 | Dismantling GCF | 1937 | GCF | Good |
| R. 46 | 15 yrs. | 1 | PGE | 1932 | DU | Poor |
| | 1 yr. | 2 | Dismantling GCF | 1936 | GCF | Poor |
| J. 28 | 2 hrs. | 1 | Plication of perforated ulcer and PGE | 1930 | Perforated DU | Poor |
| | 4 yrs. | 2 | Laparotomy | 1935 | No ulcer | Poor |
| | 2 yrs. | 3 | Dismantling GCF | 1937 | GCF | Poor |
| | 2 mos. | 4 | Pólya resection | 1938 | DU | Died (p.o.) |
| G. 55 | 1½ yrs. | 1 | PGE | 1929 | DU | Poor |
| | 5 mos. | 2 | Dismantling GCF | 1935 | GCF | Poor |
| B. 43 | 3 yrs. | 1 | PGE | 1930 | DU | Poor |
| | 5 yrs. | 2 | Dismantling GCF | 1937 | GCF | Poor |
| | 1 yr. | 3 | Billroth II | 1938 | DU | Good |
| W. 39 | 7 yrs. | 1 | PGE | 1935 | DU | Poor |
| | 2 mos. | 2 | Dismantling | 1936 | MU | Poor |
| | 1½ yrs. | 3 | PGE | 1939 | DU | Poor |
| | 4 mos. | 4 | Dismantling and resection | 1941 | GCF | Good |

TABLE VI.—CASE REPORTS*—Concluded

| Name Age in years | Duration of symptoms | No. | Procedure | Date | Lesion | Result |
|---|---|---|---|---|---|---|
| I. 43 | 6 yrs. | 1 | PGE | 1927 | DU | Poor |
| | 8 mos. | 2 | Excision of GC fistulous tract | 1934 | GCF | Poor |
| | 10 mos. | 3 | Dismantling GCF | 1936 | GCF | Died (p.o.) |
| L. 32 | 1 yr. | 1 | Perforated ulcer plication | 1932 | Perforating GU | Poor |
| | 3 wks. | 2 | PGE (2 mos. after) | 1932 | GU | Poor |
| | 5 yrs. | 3 | Dismantling and pyloroplasty | 1937 | MU | Good |
| Z. 37 | 20 yrs. | 1 | Perforated ulcer plication | 1935 | Perforating DU | Poor |
| | 4 mos. | 2 | PGE | 1936 | DU | Poor |
| S. 28 | 4 yrs. | 1 | Perforated ulcer plication | 1930 | Perforating DU | Poor |
| | 1½ yrs. | 2 | Perforated ulcer plication | 1932 | Perforating DU | Poor |
| | 1½ yrs. | 3 | PGE | 1934 | DU | Good |
| M. 41 | 1 day | 1 | Perforated ulcer plication | 1938 | Perforating DU | Poor |
| | 2 wks. | 2 | Gastric resection | 1938 | DU | Good |
| S. 71 | 15 yrs. | 1 | Excision of DU | 1934 | Perforating DU | Poor |
| | 2 yrs. | 2 | PGE | 1937 | DU | Poor |
| B. 30 | 10 yrs. | 1 | Perforated ulcer plication | 1938 | Perforating DU | Poor |
| | 2 yrs. | 2 | Gastric resection | 1940 | DU | Poor |
| H. 46 | 15 yrs. | 1 | Perforated ulcer plication | 1935 | Perforating DU | Poor |
| | 3 yrs. | 2 | Billroth II | 1940 | DU | Good |
| M. 54 | 6 mos. | 1 | Perforated DU, plication | 1934 | Perforating DU | Poor |
| | | 2 | Pólya resection | 1934 | DU | Good |
| I. 43 | 18 yrs. | 1 | Perforated ulcer plication | 1927 | Perforating DU | Poor |
| | 7 yrs. | 2 | Billroth II | 1934 | DU | Good |
| S. 23 | 7 yrs. | 1 | Perforated ulcer plication | 1931 | Perforating DU | Poor |
| | 8 yrs. | 2 | Billroth II | 1939 | DU | Poor |
| B. 42 | 17 yrs. | 1 | Perforated ulcer plication | 1939 | Perforating DU | Poor |
| | 2 mos. | 2 | Billroth II | 1940 | DU | Good |
| B. 52 | 15 yrs. | 1 | Perforated ulcer plication | 1936 | Perforating DU | Poor |
| | 15 mos. | 2 | PGE | 1938 | DU | Good |
| S. 38 | 1 yr. | 1 | Finney pyloroplasty | 1932 | DU | Poor |
| | 11 wks. | 2 | PGE | 1933 | DU | Poor |
| H. 49 | 8 yrs. | 1 | Pyloroplasty | 1932 | DU | Poor |
| | 6 hrs. | 2 | Pyloric exclusion and PGE for bleeding | 1935 | DU | Poor |
| L. 27 | 6 yrs. | 1 | Pyloroplasty and appendectomy | 1932 | DU | Poor |
| | 5 yrs. | 2 | Billroth II | 1937 | DU | Good |
| S. 53 | 1 yr. | 1 | Excision of GU and PGE | 1933 | GU | Poor |
| | 4 mos. | 2 | Gastric resection | 1939 | GU | Good |
| D. V. 39 | 12 yrs. | 1 | PGE | 1929 | DU | Poor |
| | 5 mos. | 2 | Pylorectomy | 1933 | DU | Good |
| B. 34 | 5 yrs. | 1 | PGE | 1934 | DU | Poor |
| | 1 yr. | 2 | Pyloric resection and enteroenterostomy | 1937 | DU and MU | Good |
| W. 53 | 14 yrs. | 1 | PGE | 1928 | DU | Poor |
| | 6 yrs. | 2 | Dismantling | 1934 | MU | Poor |

*All cases followed up to 1942.
DU. Duodenal ulcer. GU. Gastric ulcer. MU. Marginal ulcer. PGE. Posterior gastroenterostomy. GCF. Gastrocolic fistula.

have tended to be severe in our estimate, and most of the doubtful cases have been listed as poor results. Failure to get relief from pain, bleeding, or x-ray evidence of ulcer sufficed to make us classify a case as "poor."

Judged by these standards our results are as follows: of 53 patients the result was good in 28, or 53 per cent; poor in 18, or 34 per cent; and 7 patients died, 13 per cent.

## CONCLUSIONS

All secondary ulcers are serious problems, and reconstructive operations are attended by results that are, on the whole, not satisfactory. Therefore, patients who have secondary ulceration should first be treated conservatively on a medical regimen under careful psychiatric supervision. If these measures do not bring about improvement, operative treatment should be undertaken. The procedure that offers the best hope of success is one that eradicates the secondary lesion and also the conditions that favored the original ulcer—namely, gastric resection.

## REFERENCES


1. Alessandri, R. Arch. klin. Chir., 1903, 170: 152.
2. Allen, A. W. Surgery, 1937, 1: 338.
3. Balfour, D. Ann. Surg., 1928, 88: 548.
4. Benedict, E. Surg. Gynec. Obst., 1933, 56: 807.
5. Finsterer, H. Surg. Gynec. Obst., 1939, 68: 334.
6. Ginzburg and Mage, S. Surg. Gynec. Obst., 1938, 67: 788.
7. Graham, R., and Lewis, I. J. Am. M. Ass., 1935, 104: 386.
8. Haberer, H., von. Arch. klin. Chir., 1939, 196: 304.
9. Hurst, A., and Stewart, M. Lancet, 1928, 2: 742.
10. Lahey, F., and Swinton, N. Surg. Gynec. Obst., 1935, 61: 599.
11. Pfeiffer, D., and Kent, A. Ann. Surg., 1939, 110: 659.
12. Rife, C. S. Am. J. Surg., 1938, 40: 73.
13. Starlinger, F. Arch. f. klin. Chir., 1903, 170: 152.
14. Walter, W., and Claggett, O. Am. J. Surg., 1939, 46: 94.
15. Wright, G. Brit. J. Surg., 1935, 22: 433.
16. Zukschwerdt, L., and Eck, T. Deutsche Zschr. f. Chir., 1932, 237: 457.

# ACUTE CHOLECYSTITIS AND ITS RATIONAL TREATMENT

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A PERUSAL of the literature on abdominal surgery during the past few years indicates not only that there has been a growing interest in the subject of acute cholecystitis but also that with this increased interest there has unfortunately arisen much confusion and difference of opinion regarding its treatment. While all are agreed that the ultimate cure of the condition lies in operation, many surgeons advise "immediate" or "early" surgical intervention in order to avert such sequelae as gangrene, perforation, and peritonitis, while others, equally experienced, are just as emphatic in declaring their adherence to "delayed" operation as the treatment of choice on the grounds that under conservative management symptoms will often subside and so enable operation to be undertaken at a quiescent period with less risk to the patient.

The cause of this confusion is not far to seek, for it lies in the failure to realize and apply the important fundamental surgical principle that the basis of the rational treatment of any condition is a thorough knowledge and appreciation of the underlying pathology and its correlation with the symptomatology. In many articles concerning acute cholecystitis no mention is made of its pathology; in others, when an outline of this aspect of the disease has been attempted, no effort is made to emphasize its importance or to correlate it with the symptomatology and thus use it as the key to the rational treatment.

The result of this failure is to be seen throughout the literature by the lack of mention of specific clinical indications for operation, for the recognition of these indications as such can be based only upon a knowledge which permits of an interpretation of the symptomatology in terms of the pathology. In place of this rational approach to the problem of "when to operate" it has unfortunately become the accepted custom to attempt its solution in terms of the time factor. Thus the discussion has resolved itself into an argument as to whether operation should be undertaken as an "immediate," "early," or "delayed" procedure (terms which cannot be satisfactorily defined), disregarding the important fact that the rate of progression of the pathological changes which take place in this condition varies in each case to a greater or less extent and therefore can never bear a fixed relationship to the time factor, for in one case these changes may advance in 24 hours to a stage comparable to that which may not be reached in another for several days. It is true, since operation will be undertaken at some time or another, that the actual time of its performance will naturally fall into one of these categories, but to choose that time because of belief in respective "immediate," "early," or "delayed" operation as such instead of on the basis of specific indications for its performance is not only an irrational procedure, but is likely to lead, on the one hand, to the unnecessary performance of an emergency operation or, on the other, to a delay which might well prove fatal.

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## ETIOLOGY AND PATHOLOGY

At the outset it should be realized that there are two distinct factors playing a part in the etiology of acute cholecystitis.

The first is an acute inflammation of greater or less degree involving all layers of the gall-bladder wall, though usually most marked in the submucosa. In many cases the irritant causing this inflammation is of the infective type but in others no evidence of infection can be found on competent bacteriological investigation, as pointed out by Andrews. It follows that in such cases the irritant is of the noninfective type, the most obvious being the trauma inflicted upon the friable mucous membrane by a stone or stones, especially one suddenly impacted in the region of the cystic duct. In recent years another irritant of this type suggested as a possible cause of the inflammatory reaction consists of the ferments of pancreatic juice which has reached the gall bladder by reflux (2, 12).

The second factor is acute obstruction to the outlet of the gall bladder. This is due either to the sudden impaction of a stone in or near the cystic duct, as in most cases, or to the occlusion of this duct by inflammatory edema. The importance of this factor lies in the fact that the special characteristics of acute cholecystitis, both pathological and symptomatic, as we have come to recognize them, arise only when such obstruction takes place. The writer suggests, therefore, that if this condition were to be designated "acute obstructive cholecystitis" not only would this be

correct terminology but it would serve the additional purpose of forcefully reminding the surgeon of a factor which often plays a more important rôle than inflammation in deciding the outcome of the pathological changes.

Since the outlet of the gall bladder is so small, obstruction, should it occur at all, is likely to be complete and even if only partial it is sufficient to interfere materially with the emptying of the organ. In milder cases, however much the assumption of the occurrence of a partial obstruction only may be correct, there seems little room for doubt that in those more advanced, that is, those in which the pathology has been progressive, the obstruction is complete. As will be seen later, the importance underlying obstruction depends not so much upon its degree, for there is little actual difference between the partial and complete varieties because of the small size of the outlet in which it is occurring, but upon whether it will, or will not, be relieved.

It is thus necessary that we should know what changes may follow an acute obstruction of the gall bladder. Many years ago Rutherford Morison, a great teacher, drew attention to the fact that when a stone suddenly blocks the neck of the viscus, one of three typical conditions follows, depending upon the amount of bile present in the gall bladder when the obstruction takes place (7). These are: (1) The gall bladder becomes slowly distended by its own secretion and forms a chronic, painless lump in the right hypochondrium (hydrops of the gall bladder). (2) This distended gall bladder may become the seat of inflammation and there is a tender lump in the right hypochondrium (empyema of the gall bladder). (3) The distended gall bladder becomes gangrenous (gangrenous cholecystitis).

Morison added the explanation that in hydrops the gall bladder has been emptied by its contraction before impaction of the stone and after the impaction it became distended with its own secretion, while in gangrenous cholecystitis the stone became impacted as a first step, just as the plug in an emptying bath may be swept into its outlet, and the gall bladder thus remained full of infected bile.

It is with the third condition, that is, the acute cholecystitis which may terminate in gangrene, that we are here particularly concerned, although empyema of the gall bladder may be so acute as to be clinically indistinguishable from it.

The mechanism whereby such a distended gall bladder may become the seat of gangrene is described in an important general principle formulated by Morison (8). This principle states that if, in any hollow muscular viscus, active inflammation is superadded to obstruction, the intravisceral tension increases and may become so acute as to interfere with the circulation to such an extent that partial or total gangrene ("tension gangrene") of the involved viscus, to be followed by rupture and extravasation of its contents, will take place. While the importance of this general principle is obvious, its value is further enhanced by the fact that it can be applied to any hollow muscular viscus.[1]

In acute cholecystitis the gall bladder is the seat of this combination of acute obstruction and inflammation and the essential pathology is that which is indicated in Morison's principle. The augmentation of the fluid contents of the gall bladder which results in an increase in the intravisceral tension is brought about by both exudation and transudation into the lumen, the former a result of the inflammatory reaction, the latter through the congestion of the submucosal and mucosal veins and capillaries consequent upon compression of the blood vessels in the wall during the forcible contractions of the unstriated muscle, these contractions representing Nature's method of attempting to overcome the obstruction. This compression may also result in extravasations of blood from these veins and capillaries claimed by some to be "infarcts." It is possible that in some cases the musculature passes into a state of tonic spasm and this occurrence, should it take place, would lead to increased severity of these vascular changes. Exudation and transudation also take place into the composite tissues of the wall of the gall bladder, giving rise to the edematous thickening which is such a marked feature of acute cholecystitis. Thus both the inflammatory and obstructive factors are concerned in the production of the increase in the intravisceral tension. While it may be difficult to estimate the relative importance of the rôle played by each of these factors, yet in some cases the predominance of the inflammatory factor may be readily discernible, both to the naked eye and microscopically, especially when the irritant causing the inflammation is of the infective type (Fig. 2). On the other hand, in cases in which acute inflammatory changes of mild degree only are found on microscopic examination of the excised gall bladder and its contents, inflammatory exudation can have played but a minor rôle in effecting the increased

[1] It is of interest that recent articles on the subject of acute appendicitis indicate an increasing realization of the important part played by obstruction and increased intravisceral tension in a disease hitherto often regarded as being solely of an inflammatory nature. What is not realized yet, however, is that this disease is but one example of the "tension gangrene" principle taught for many years by the late Professor Morison and applicable to all the hollow muscular viscera (Fig. 1).

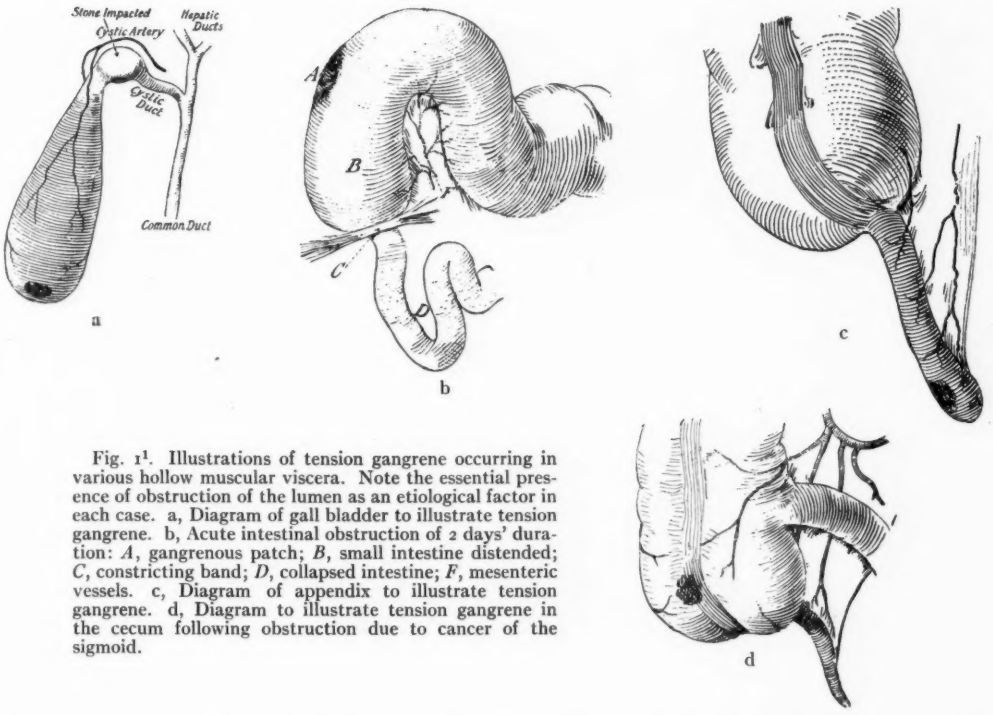


Fig. 1[1]. Illustrations of tension gangrene occurring in various hollow muscular viscera. Note the essential presence of obstruction of the lumen as an etiological factor in each case. a, Diagram of gall bladder to illustrate tension gangrene. b, Acute intestinal obstruction of 2 days' duration: *A*, gangrenous patch; *B*, small intestine distended; *C*, constricting band; *D*, collapsed intestine; *F*, mesenteric vessels. c, Diagram of appendix to illustrate tension gangrene. d, Diagram to illustrate tension gangrene in the cecum following obstruction due to cancer of the sigmoid.

intravisceral tension, the factor chiefly responsible for this being the transudation of fluid into the lumen consequent upon the repeated vascular compression by the forcible muscular contractions (Fig. 4). Because the pathological state of the gall bladder can thus vary considerably in acute cholecystitis, attempts have been made to classify this condition into various pathological types (10), but it should be remembered that these variations represent, not separate pathological entities, but only different degrees of severity of a disease consequent upon the same underlying pathology.

The increasing distention of the obstructed gall bladder results in the squeezing of the blood vessels in the tensely stretched wall, thus interfering with the passage of blood through them, and may eventually lead to their complete occlusion with death of the tissues supplied by the vessels so affected. The gangrene which is the outcome of this type of mechanical interference with the blood supply has certain definite features. It always commences at a spot farthest from the source of vascular supply, for this area is naturally the most vulnerable to such interference, and so, in the case of the gall bladder, it is first observed at the fundus. It appears as a black or grayish, rounded or oval, patch which steadily spreads, its extent depending upon the amount of vascular bed occluded. As might be expected, the mucosa is always the first and most affected, and it is not uncommon, therefore, in early cases to find gangrene of this layer present although the rounded patch, indicating a spread of the gangrene to involve the whole thickness of the wall, has not made its appearance (Fig. 2). It should be noted that gangrene may also take place at the site of an impacted stone from direct pressure. Figure 1 illustrates examples of tension gangrene in various hollow muscular viscera and is reproduced to stress its importance in surgery and the possibility of its occurrence, not only in the gall bladder, but in any of the hollow muscular systems of the body.

The theory of Denton that the vascular interference in acute cholecystitis is due to circulatory stasis consequent upon obstruction of the cystic vein and lymphatics by pressure of the stone

[1](Reproduced from *An Introduction to Surgery.* By Rutherford Morison and Charles F. M. Saint. 3rd ed., 1935, by permission of the publishers, John Wright and Sons, Bristol.)

impacted in the cystic duct is mentioned because many recent writers appear to have accepted its validity without question, although Kreider's work disproved it completely on anatomical grounds alone. Moreover, in some cases no stone is present to account for the vascular interference and, in addition, if a stone is impacted in the duct, it is well known that cholecystostomy will relieve the vascular interference even if this stone is inadvertently left behind at operation—it would fail to do so if the vascular interference was due to pressure by the stone upon the cystic vein. Finally, this theory can never explain the vascular interference found in other obstructed hollow muscular viscera when the agent obstructing the viscus is so far removed from the main venous and lymphatic trunks that the possibility of it exerting pressure upon these structures does not arise as, for example, in the appendix or cecum (Fig. 1). Its failure to do so at once reveals the limitations imposed by regarding the gall bladder as an isolated entity instead of applying to it the principles governing the hollow muscular viscera in general.

The termination of an attack of acute cholecystitis, whether by resolution, fibrosis, partial destruction or total destruction of the gall bladder, would appear to depend more on the obstructive than on the inflammatory element of the pathology, for when the gall bladder succeeds in emptying itself the attack usually subsides. In other words, if the obstruction is relieved, with consequent lowering of the intravisceral tension, the more serious terminations of partial or total gangrene are unlikely to occur. This is borne out clinically, for these more serious terminations never occur except in cases in which the gall bladder is tensely distended, indicating a failure on the part of Nature to have removed or otherwise overcome the obstruction and so to have relieved the increased intravisceral tension.

### THE RATIONAL TREATMENT

A study of the pathology of acute cholecystitis makes it clear that once the etiological factors already discussed have come into play and established the disease, the outcome depends upon whether or not the resultant increased intravisceral tension will be relieved. Should the condition be left to Nature, there are two possibilities whereby the tension may be relieved, the first being that the obstruction may be overcome or removed (e. g. the dislodgement of a stone obstructing the neck of the gall bladder) and so allowing the escape of the contents through the natural passages; the second, that their escape will be provided for through a rupture of the wall after gangrene has occurred, this catastrophe representing the natural cure of increased tension in any hollow muscular viscus in the presence of an obstruction which Nature herself is unable to remove or otherwise overcome. Should the first possibility occur, then the need for surgical intervention as an emergency measure does not arise, for the patient will recover from the attack. In such a case, elective surgery can be undertaken at a later date. It is in the prevention of the second possibility, which materially increases the chances of a fatal outcome, that surgery assumes its important rôle and here, following the lead Nature herself gives, *the rational treatment consists of relieving the increasing intravisceral tension when it has become apparent that she is unlikely to do so herself except by gangrene and perforation.* The clinical manifestations which warrant this assumption, that is, that the pathology has progressed to such a stage, and which therefore indicate the need for surgical intervention if the more serious terminations of the disease are to be prevented, will be considered presently. Judging from the literature, so far as the writer is aware the existence of this pathological stage, as such, has not been realized, although all cases which have progressed to gangrene must of necessity have passed through it. Once it has been generally accepted and its clinical recognition established, then a definite advance will have been made in the management of acute cholecystitis, for this knowledge will tell us clearly the time when operation should be undertaken and so simplify a decision which at present is the subject of much confusion and difference of opinion.

Relief of the tension may be accomplished either by drainage of the gall bladder or by its actual removal, the type of procedure performed being decided at operation, rather than by routine, such factors as the general condition of the patient, the local findings at operation and the ability and skill of the surgeon all having to be taken into consideration in making the decision.

### SYMPTOMATOLOGY IN RELATION TO THE PATHOLOGY

It is not proposed to describe in detail the symptomatology of acute cholecystitis but rather to discuss its special significance as a guide to the progress of the disease and thus to the time when operation should best be undertaken.

It has been pointed out that the disease may progress to a stage when the intravisceral tension has increased to such a degree that, unless it is relieved by surgical means, the pathological

changes are more likely to progress than retrogress, that is, this tension will continue to increase and lead to more and more interference with the blood supply to the gall-bladder wall until gangrene finally supervenes. From the surgical standpoint, therefore, it is in particular with the clinical recognition of this stage that we are concerned. While we are enabled to follow the progress of any case by observation of certain clinical manifestations, both general and local, the writer has found that there is one in particular, the development of which in the course of a case of acute cholecystitis, transcends all others as an indication that this stage has been reached. It is:

*The development of a tender, palpable mass in the right upper quadrant.* If noted early in its development, this mass will present the typical characteristics of a distended gall bladder as regards shape, definition, dullness on percussion and relations. Later, with extension of the inflammation to the visceral peritoneum the gall bladder usually becomes buried in omentum (this structure acting in its capacity of abdominal policeman and as such endeavoring to exclude the source of mischief from the general peritoneal cavity) and the mass, while retaining the gall-bladder relations, loses the shape and definition of the free gall bladder and at the same time tends to become more fixed.

Should such a gall bladder be examined, it will be found to present an appearance markedly different from that of the normal viscus (Figs. 3 and 4). It is enlarged, the increase in size being partly due to the thickening of the wall by edema but mostly to distention beyond its normal capacity by the increased volume of its fluid contents which may vary from dark looking bile in some cases to frank pus in others. In the early stages, the wall is of a reddish hue and later becomes a plum-blue color resembling that of strangulated bowel, while later still the black or gray color characteristic of gangrene makes its appearance beginning, as noted previously, at the fundus. It is tense, in contradistinction to the comparative laxity of the normal, though distended, gall bladder. If a small incision be made in the fundus, the contents will be expelled forcibly, indicating the increased tension under which they have been present in the viscus, in marked contrast to the nonexpulsive, even flow of bile that occurs from a distended normal gall bladder similarly opened. It is obvious that the gall bladder could become tensely distended in such a manner only in the presence of an obstruction of its outlet preventing the escape of its increasing contents through the cystic duct. Inflammation, in the absence of obstruction, could not produce this tense distention of the viscus, for the exudate poured into the lumen would be able to escape through the cystic duct. What is the significance of this clinical finding? In the first place, it generally settles whatever doubts there may have existed regarding the diagnosis up to the time of its appearance and, second, it has a bearing of the utmost importance on prognosis and treatment.

Recovery, without operation, can be accomplished only by the escape of the fluid contents of the gall bladder through the cystic duct, the increased intravisceral tension being thereby relieved. According to the nature of the obstruction, this would imply such occurrences as: extrusion of an impacted stone through the cystic duct into the common duct; disimpaction of the stone which is then free to fall back into the lumen of the gall bladder; diminution of the edema of the mucosa to an extent such as will allow the passage of the contents past a stone in the outlet or, if no stone is present, will open up the previously closed cystic duct; relaxation of muscular effort which may lead to actual dilatation of the duct, with a similar result.

The outcome of these considerations is the question: in view of the pathological significance of this clinical stage of the disease, what are the chances of such spontaneous recovery and what are those of progression, *once it has been reached?* The writer is of the opinion that when this stage has been reached the intravisceral tension has become so great that the time has passed when such occurrences as those here mentioned are likely to take place. That the disease has actually progressed to this stage appears to him to indicate either that an obstructing stone has become so firmly impacted that it cannot be moved by natural means or that edema occluding the outlet of the gall bladder is progressive in character, as otherwise this stage would not have been reached. The writer's contention, therefore, based upon the pathology and his clinical experience, is that to expect or hope that spontaneous recovery will take place, once this stage has been reached, can best be described as wishful thinking and that if the increased intravisceral tension is not relieved by surgical intervention, then progression, with its serious terminations, is much more likely to be the outcome. Thus it is considered that this stage of acute cholecystitis, as typified by the development of a tender, palpable mass in the right upper quadrant of the abdomen in the course of the disease, is one of crucial importance and significance since it constitutes

a clear indication that the time has arrived when operation should be undertaken as soon as possible with the object of relieving the increased tension within the gall bladder.

It is realized, however, that no doubt some cases which have reached this stage do recover without operation and while this is so, yet, apart from the pathology indicating the probability of progression, another cogent reason for operating at this stage is that it is not possible to foretell which case will recover and which will not. It is therefore surely wiser to play for the safety which lies in operative relief of the intravisceral tension since progression to gangrene, even without perforation, diminishes the patient's chances of recovery. There are many surgeons who hold the opinion that operation at this, necessarily acute, stage of the disease, far from being a safe procedure, will assuredly result in a formidable mortality. The writer has never felt that this should be so in the hands of any competent surgeon and, in view of his personal experience (q. v.), he cannot subscribe to this opinion. The high mortalities reported in some series of cases in which operation was done while the disease was in the "acute" stage appear to him, in many instances, to represent the penalty of delay, this stage having been allowed to last too long through the hope or expectation that recovery would take place under conservative measures. Thus in such cases the cause of death is not the operative procedure, *per se*, although this is blamed statistically, and quite wrongly, for it, but the fact that operation was undertaken at too late a pathological date to obtain the desired successful result.

It is sometimes reported that in acute cholecystitis, when a greatly enlarged, distended, and perhaps gangrenous gall bladder, enveloped by omentum, has been found at operation, the presence of a mass in the right upper quadrant could not be elicited on clinical examination. The failure to determine before operation the presence of a mass in such a case is generally attributed to interference with satisfactory palpation by the tenderness and rigidity of the overlying musculature. However, because such a mass results in an area of dullness occurring in an otherwise normally resonant portion of the abdomen, and because the rigidity will often be found insufficient to prevent the appearance of a swelling which can be seen by careful observation in a good light, it may be said that, on the whole, when a gall bladder has become the seat of the pathological changes referred to, the presence of a mass in the right upper quadrant of the abdomen will not usually escape detection by the careful examiner. Should it happen to do so, then the determination of the pathological progress of the disease must necessarily depend upon the interpretation which is made of other clinical manifestations, the chief among which will be discussed in the following paragraphs.

The development of rigidity of the musculature in the region of the gall bladder is a physical sign of considerable importance since it represents the reaction of the abdominal wall to irritation of the parietal peritoneum. Not only may it be the first sign to point to disease of the gall bladder as the cause of symptoms of previously doubtful origin and thus prove of definite diagnostic value, but, more important still, it also indicates a spread of the pathological process beyond the confines of the gall bladder itself. Consequently, it is the signal for intent observation for spread of the rigidity or the development of a mass under the rigid muscles. A spread of the rigidity, even if apparently no mass becomes manifest, in the writer's opinion, would indicate the advisability of operative interference on the grounds that it signifies a steady progression of the pathological process. In most cases, other signs and symptoms will furnish confirmatory evidence of this progression.

The behavior of the pulse is of the utmost importance, for a continuous increase in its rate is one of the most frequent accompaniments, and therefore one of the most certain indications, of a progressive pathology.

The temperature chart must be mentioned as some writers advise that operation should not be undertaken until the temperature has subsided, thereby inferring that great reliance can be placed upon this single clinical feature as a prognostic guide. Unfortunately, such advice is not always accompanied by equally emphatic counsel urging the necessity of always considering the temperature in conjunction with other clinical manifestations, for a falling temperature may indicate, not improvement, but that the patient's resistance is being overwhelmed by a general toxemia consequent upon the local condition. Under these circumstances it is the progression of one or more of these other clinical manifestations which will indicate what is happening. Moreover, in the more severe cases the temperature may never rise at all and, indeed, may be subnormal. As the writer's experience of acute cholecystitis has grown he has become more and more impressed with the unreliability of the behavior of the temperature as a guide either to the general or local condition of the patient or to the optimum time for operative interference.

TABLE I.—AGE AND SEX INCIDENCE IN 44 OPERATIVE CASES OF ACUTE OBSTRUCTIVE CHOLECYSTITIS*

| Decade | Males | Females | Total |
|---|---|---|---|
| 10–19 | — | 1 | 1 |
| 20–29 | — | — | — |
| 30–39 | 3 | 2 | 5 |
| 40–49 | 2 | 5 | 7 |
| 50–59 | 3 | 7 | 10 |
| 60–69 | 7† | 11 | 18 |
| 70–79 | 1 | 1 | 2 |
| 80–89 | — | 1 | 1 |
| Totals | 16 | 28 | 44 |

*The chief indication for operation in each case was the finding of a tender, palpable mass in the right upper quadrant.
†The only fatality occurred in a man, aged 66 years, following cholecystectomy.

The value of the total and differential leucocyte counts, in some surgeons' minds, appears open to question but the writer has usually found these determinations, when repeated, to tally fairly closely with the clinical progress of a case. As with the temperature, we must remember that a falling leucocyte count, coincident with simultaneous progression of other clinical manifestations, suggests a failing resistance on the part of the patient.

The type of case referred to by Heuer, Mentzer, Touroff, and others, in which an advanced pathological process, with or without a fatal outcome, was accompanied by deceptive minimal symptomatology, has never been encountered by the writer.

## PERSONAL EXPERIENCE

Since 1930 the writer has had occasion to operate upon 44 cases of acute cholecystitis and these will presently be discussed in some detail. Of these operations, 25 were performed at the Royal Victoria Infirmary, Newcastle-on-Tyne, 9 at the Knight Memorial Hospital, Blyth, Northumberland, 4 in private nursing homes, and 6 at the Santa Barbara Cottage Hospital (Table I). This series, though small in number in comparison with those which emanate from hospitals, has the advantage of representing the experience of a single surgeon in that his opinion alone was responsible for advising the operations and these were all performed by him. Those larger series, referred to, usually represent the work of several or many surgeons who may hold varying opinions on the pathology and treatment of acute cholecystitis. In consequence these reports resolve themselves largely into statistical surveys and the conclusions which are drawn from them usually represent nothing more or less than the reviewer's interpretation of the significance of the figures presented.

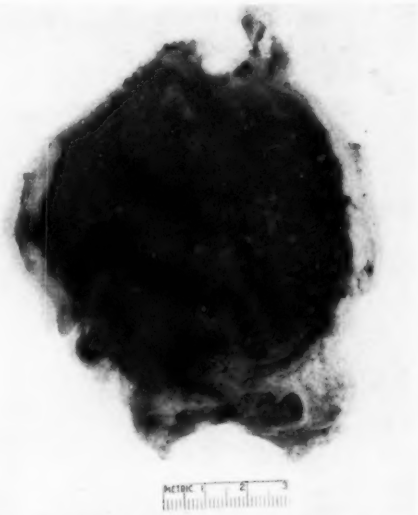

Fig. 2. The gall bladder in a case of acute obstructive cholecystitis, showing gangrene of the mucosa. The contents consisted of purulent, evil-smelling bile under great tension. Escherichia coli and a nonhemolytic streptococcus were cultured from both bile and gall-bladder wall and microscopic examination of the latter showed marked evidence of acute inflammatory change. The wall was relatively thin at the fundus, and a patch of gangrene would soon have appeared in this region. A small stone was impacted at the outlet. Onset of symptoms only 48 hours before operation.

In each of these 44 cases the chief indication for operation was the finding of a tender, palpable mass in the right upper quadrant of the abdomen, the pathological significance of which clinical manifestation has already been discussed at some length. This physical sign was present in 28 patients when these were first seen either in consultation or on admission to hospital, and immediate operation was advised and undertaken. By an immediate operation is meant one which is undertaken as soon as it can be arranged after the decision to operate has been made, that is, after the short interval which is all that is necessary to carry out whatever preoperative measures may be deemed advisable, such as the administration of sedatives and intravenous therapy, gastric lavage, etc. In the 16 remaining cases, the patients were under observation for a length of time varying from hours to 8 days (11 cases 3 days or less) before this sign became manifest. When,

Fig. 3. Exposure of the gall-bladder region through a Kocher incision (inset) in a case of acute obstructive cholecystitis. Shows the characteristic appearance of the omentum enveloping the gall bladder and thus shutting it off from the general peritoneal cavity. (From a photograph taken at operation.)

but not until, it did so, immediate operation was advised and undertaken. It is emphasized, therefore, that the decision of "when to operate" was not in any way related to any belief or general rule regarding advisability of respective "immediate," "early," or "delayed" operation as such, but was based entirely upon the development of what are considered specific indications for operative intervention, the chief among these being the finding of a tender, palpable gall bladder, while other signs such as a spreading rigidity of the overlying muscles and an increasing pulse rate were usual accompaniments furnishing confirmatory evidence of the progressive nature of the pathological process.

The only death occurred in the last case of the series following cholecystectomy, so that in 43 consecutive cases patients were operated upon without a fatality. This fact is of importance if for no other reason than proving the fallacy of the statement, often encountered, that operation in the acute stage of acute cholecystitis is likely to be associated with a forbidding mortality rate. However, it is not the writer's wish that by this fact shall be judged the principles of treatment, outlined in this communication, which governed the management of these cases. If they are to be accepted, rather let it be on the grounds, already emphasized, that they are based on the only rational method of approach to the treatment of this or any other acute surgical condition, namely an understanding of the pathology and its correlation with the symptomatology. Had other deaths occurred to mar this series from the statistical standpoint through circumstances which could reasonably be considered beyond surgical control, such as incidental disease or pathology already too advanced when first seen, such fatalities would not in any way have altered his adherence to, and teaching of, those principles. Indeed, since acute cholecystitis is a disease most prevalent in the later decades of life—in the present series of 44 cases, 31, or 70.5 per cent, were over 50 years of age and 21, or 47.7 per cent, were over 60 (see Table I)—it is unlikely that every case will survive, irrespective of whether operation is performed or not or when it is undertaken. Thus a comparison of the mortality rates as the deciding factor on which to base an opinion as to the most propitious time for operation to be undertaken in this acute surgical condition may lead to conclusions which may be not only false but frankly dangerous.

Gangrene of the whole thickness of the wall had occurred in 5 of the 28 cases in which a palpable mass was present when first seen and upon which immediate operation was performed. In one of these cases perforation had occurred but the envelopment of the gall bladder by the omentum had prevented the soiling of the general peritoneal cavity. No instance of gangrene affecting the whole thickness of the wall occurred among those patients who developed a palpable mass while under observation and who were operated upon immediately following the discovery of this clinical manifestation but, in several instances, gangrene of the mucosa alone was found to have taken place (Fig. 2).

The frequency with which stones are found to be the cause of obstruction in acute cholecystitis is well exemplified in the present series, for they were responsible for its occurrence in 40, or 91 per cent, of these 44 cases. In the 4 remaining cases no stones were present.

Cholecystostomy was performed in 32 cases and cholecystectomy in the 12 remaining, the preponderance of cholecystostomies being due to the fact that they largely represent the writer's earlier operative experience. The investigation carried out some years ago by the writer (9) on patients

previously subjected to cholecystostomy convinced him that, after an attack of acute cholecystitis, the gall bladder will only resume reasonably good function in a minority of cases and thus converted him to the belief that when the patient's general condition is good and the local findings are such that cholecystectomy can be performed satisfactorily, this is the operation of choice. Consequently, when operation is done in a case of acute cholecystitis, it is now his practice to remove the gall bladder unless this procedure is contraindicated by the presence of some general or local condition, in which case drainage only, with removal of whatever stones may be present, is performed.

The writer has no means of knowing the number of cases, diagnosed provisionally as acute cholecystitis, which have been under his care and which recovered from their attacks without operation, but they certainly exceed in number those upon which operation was performed. In no case which, after the writer's first clinical examination, he decided to observe, did a fatality occur (the only one in this series occurred in a man who already had a tender, palpable mass when first seen and immediate operation was advised), for they either recovered under the conservative measures instituted or, under these, progressed to the stage in which a tender, palpable mass developed and immediate operation was then advised and undertaken successfully. Thus, the patients who recovered without operation, and who formed the majority of those observed, consisted only of those who never progressed to this stage, indicating that, until this stage is reached, the possibility of recovery is sufficiently great to warrant the adoption of conservative treatment unless one is dealing with the exceptional case in which, in spite of a failure to detect a palpable mass, other clinical manifestations indicate a progressive pathological condition. The writer, therefore, considers that to insist that every patient should be operated upon as an emergency is just as erroneous as to declare that all patients should be treated on the "delayed" plan. In no patient in whom a palpable mass developed were conservative measures adopted or continued in contemplation of recovery of the patient from the attack before operation was undertaken—all such patients were operated upon according to the principles of treatment outlined in this communication as no grounds were present for considering any one of them too great a surgical risk. Hence it is impossible to know what results would have been obtained by conservative treatment in these 44 cases after the condition had progressed to this stage. However, the writer has no doubt (when recalling to mind many of those tense, angry-looking gall bladders found at operation) that this method of treatment would not have yielded nearly such satisfactory results as those, already presented, obtained by operation undertaken at this stage of the disease in accordance with the dictates of the rational treatment.

Fig. 4. Same case as in Figure 3 showing the omentum peeled off the gall bladder which is grossly enlarged, tensely distended and has a dark colored, thickened wall. The contents consisted of nonpurulent bilious fluid under great tension. Microscopic examination of the wall showed acute inflammatory changes of only minor degree. No stones were present. The fundal mucosa was already gangrenous although only 36 hours had elapsed between the onset of symptoms and operation. (From a photograph taken at operation.)

## SUMMARY

The etiology, pathology, and symptomatology of acute cholecystitis are discussed and from the consideration of these aspects of the disease the following appear to be its outstanding features:

1. While the pathological changes which occur in the gall bladder result from the presence of two factors, namely, acute obstruction of its outlet and acute inflammation of its wall, the rôle played by the former is of such importance as to suggest the desirability of designating the disease "acute obstructive cholecystitis."

2. The essential pathological feature is an increase in the intravisceral tension in the gall bladder, the result of this combination of acute obstruction and inflammation occurring in it. This tension may become so acute as to interfere with the blood supply and may do so to such an extent that gangrene ("tension gangrene") of the gall bladder, followed by rupture and extravasation of its contents, will take place, this catastrophe representing Nature's method of relieving the increased tension within the gall bladder in the presence of an obstruction of its outlet which she is unable to remove or otherwise overcome. Should Nature succeed in overcoming the obstruction, then the contents of the gall bladder can escape by the natural passages, leading to relief of the increased intravisceral tension and consequent recovery of the patient from the attack.

3. The rational treatment aims at the prevention of gangrene, and thus of the possible complications of rupture and extravasation, by relieving the increased intravisceral tension through surgical intervention should the disease progress to the stage when it has become apparent that Nature is unlikely to succeed in her efforts to remove or overcome the obstruction.

4. The most important single clinical manifestation indicating that the disease has progressed to this stage and which therefore indicates the necessity for immediate relief of the increased intravisceral tension in the gall bladder by surgical intervention as the most certain means of preventing further progression of the pathological changes to the termination of "tension gangrene," is the development of a tender, palpable gall bladder during the course of the disease.

A series of 44 personal cases is presented in which operation was undertaken in accordance with the dictates of the rational treatment. Only one death occurred.

## REFERENCES


1. Andrews, E. Arch. Surg., 1935, 31: 767–793.
2. Colp, R., Gerber, I. E., and Doubilet, H. Ann. Surg., 1936, 103: 67-76.
3. Denton, J. Arch. Surg., 1924, 14: 1–13.
4. Heuer, G. J. Ann. Surg., 1937, 105: 758–764.
5. Kreider, P. G. Surg. Gyn. Obst., 1933, 57: 475–482.
6. Mentzer, S. H. Surg. Gyn. Obst., 1932, 55: 709–716.
7. Morison, Rutherford. Abdominal and Pelvic Surgery for Practitioners, 2d ed., p. 67. New York: Oxford University Press, 1926.
8. Morison, Rutherford, and Saint, Charles F. M. An Introduction to Surgery, 3d ed., p. 231. Baltimore: William Wood & Co., 1935.
9. Saint, James H. Brit. J. Surg., 1935, 33: 299–326.
10. Taylor, F. Surg. Gyn. Obst., 1936, 63: 298–307.
11. Touroff, A. S. W. Ann. Surg. 1934, 99: 900–913.
12. Wolfer, J. A. Surg. Gyn. Obst., 1931, 53: 433–447.

# A SIMPLIFIED ANASTOMOSIS FOR RESECTION OF THE DUODENUM AND HEAD OF THE PANCREAS

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THE radical resection of tumors of the duodenum, ampulla of Vater, and head of the pancreas involves comparable problems in the restoration of the gastrointestinal, biliary, and pancreatic functions. This procedure is not common, for Hunt's recent report lists only 124 instances of surgical removal of cancer in the periampullary region. The early efforts to perform this operation resulted in such a high mortality and such frequent complications that even the most courageous surgeon hesitated to attempt it. This attitude is expressed by Moynihan when he said that the cases in which patients were operated upon "serve to show that the mechanical difficulties of the operation are well nigh insuperable, and that if boldness and good fortune are the operator's gifts, the result to the patient hardly justifies the means." This feeling prevailed for 30 years until in 1935 Whipple, Parsons, and Mullins reported their fundamental observations and recorded success with a two stage operation. This stimulated other surgeons to attempt the procedure.

The original operations for resection of the pancreas were done in one stage. The first successful resection of the ampulla of Vater with reimplantation of the ducts done by Halsted in 1898 was likewise a one stage procedure. But early attempts at a two stage removal were made by Mayo, Savue, and experimentally by Coffey. Preliminary cholecystostomy, cholecystenterostomy, or choledochoenterostomy were used with or without gastroenterostomy at the first stage. The second stage involved the division of the biliary and pancreatic ducts which were ordinarily reimplanted into the intestine. Coffey suggested making a funnel of tissue from two loops of jejunum to cover the cut surface of the pancreas and so prevent leakage. Whipple, Parsons, and Mullins eliminated anastomosis of the pancreatic ducts and demonstrated that the pancreas could be left unattached without causing leakage or subsequent digestive disturbance. This is stated in their first principle that "after resecting the descending limb of the duodenum with the pancreas wide of the growth no attempt should be made to re-establish the continuity of the duodenum or of the pancreas with the intestine."

One fault of this operation was the development of cholangitis from the cholecystgastrostomy. Brunschwig in 1937 used cholecystjejunostomy. In 1938 Whipple (14) described an antiperistaltic cholecystjejunostomy of the Roux type which eliminated much of the hazard of ascending infection into the biliary tract. The effect of antiperistalsis on the intestinal function was demonstrated by Mall and was used by Mann in physiological experiments. Its adaptation for cholecystenterostomy is an improvement in the method.

Establishment of these principles of pancreaticoduodenectomy naturally led to slight variations in technique; one of which is the use of a single stage operation. This has the advantage of a clear field with normal anatomical relations undisturbed by adhesions from a previous operation. It is only applicable in a limited number of patients who are good surgical risks and who do not have severe, long standing jaundice. Horsley describes a one stage resection in which he anastomosed the distal cut end of the duodenum to the common bile duct. Trimble, Parsons, and Sherman believe that the resection can be done "with the greatest chance of success if the operation can be done in one stage." They used an end-to-side gastrojejunostomy. In the case here reported still another method of anastomosis was used, that of gastrojejunostomy and antiperistaltic cholecystojejunostomy which reduces the intestinal suture lines from 5 to 2, apparently a minimum (Fig. 1).

This case is reported primarily to illustrate a technical change in the operative procedure so the history, findings, and course will not be given in detail.

## CASE REPORT

B.M., No. 185146, a 56 year old married housewife, was in good health until 1 year before admission when she developed burning and tenderness in her epigastrium associated with easy fatigability and exertional dyspnea. There had been no vomiting, jaundice, or change in the stools. A careful review of the past history was noncontributory.

Physical examination showed a thin, anemic looking, chronically ill, middle aged white woman who was alert and co-operative. There was a soft systolic murmur over the precordium with an otherwise normal cardiac examination

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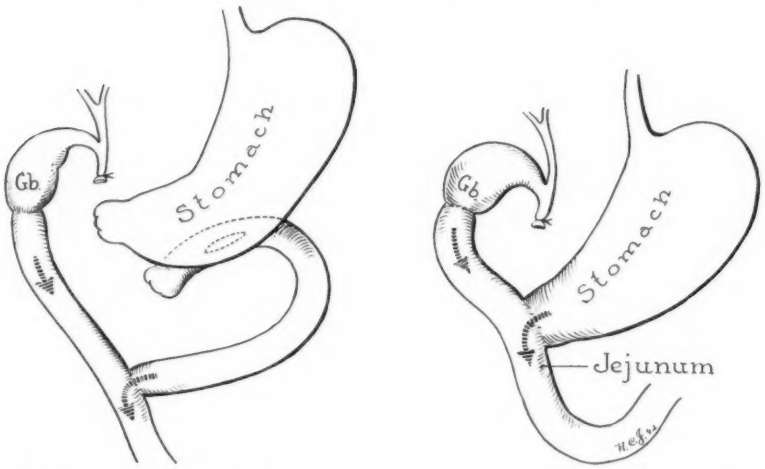


Fig. 1. A diagrammatic line drawing in which the anastomoses done in the two stage operation of Whipple, a, left, is compared with the simplified anastomosis, b, right, herein described. Note that the physiological principles of both are the same.

and a blood pressure of 110/70. In the epigastrium just to the right of the midportion, tenderness was present on deep palpation but no mass could be felt. The remainder of the examination was negative. Gastrointestinal roentgenograms showed fixation and infiltration of the duodenal loop which suggested a mass lying in this region. The impression was "carcinoma of the head of the pancreas or a mass originating in the duodenal loop."

The patient was quite anemic with a hemoglobin of 5 grams, so she was prepared for operation over an 11 day period by rest in bed, high caloric diet, iron and liver, and 6 transfusions totaling 2900 cubic centimeters of whole blood.

Operation was done December 11, 1941, under ether anesthesia. A tumor was found on the posterior wall of the descending duodenum invading the head of the pancreas but without discernible metastases in the liver. The cleavage plane under the pancreas was followed for a short distance when a hard gland was felt beyond the aorta so this dissection was stopped and a plane developed by freeing the areolar tissue off the vena cava and aorta. This passed behind the gland. There were large soft glands along the gastrohepatic omentum but these could be removed by cleaning all tissue off the bile duct, hepatic artery, and portal vein. Palpation of the pancreas showed the head invaded but division at the neck would certainly excise all involved tissue. The duodenum was infiltrated by tumor in its descending portion and appeared to be attached to the pancreatic growth in its third portion. It was decided to do a bloc dissection starting below along the vena cava and aorta and above at the bifurcation of the hepatic bile duct including in this all of the duodenum and the head and uncinate process of the pancreas (Fig. 2).

The stomach was divided near the pylorus and the proximal part turned back out of the way. The gland bearing tissue of the gastrohepatic omentum was dissected downward. The common bile duct and superior pancreaticoduodenal artery were ligated and divided. Next the transverse colon was lifted up, Treitz's ligament was divided and the duodenojejunal junction was mobilized in the manner described by Lahey. The colon was replaced, and, working in front of the transverse mesocolon, we freed the third and fourth parts of the duodenum by lifting up the middle colic and superior mesenteric vessels and rolling the bowel from beneath them. The duodenojejunal junction was divided and the distal jejunum was turned back out of the way. The inferior pancreaticoduodenal artery was ligated and the head and uncinate process of the pancreas were mobilized. This left the mass of tissue attached only by the neck of the pancreas which was then divided. Here an unexpected difficulty arose, for the neck of the pancreas was found to be only a thin sheet of tissue which could not be beveled in a V for inversion. The cut surface was sutured as carefully as possible, however, the closure was not completely satisfactory.

This extensive operation was made easier by the assistance of Dr. Stanley Widger, our surgical resident, but even so the amount of tissue removed required a prolonged dissection. All during the operation we were wearied by the thought of the gastrointestinal anastomosis to come. When the time arrived to reconstruct the digestive tract I suggested that time could be saved by attaching the open end of the proximal jejunum to the gall bladder and implanting the open end of the stomach, end-to-side, into the bowel below (Fig. 3). This was done and when it was completed the abdomen was closed without drainage by the use of silk for suture material.

The patient made a satisfactory recovery until her 7th postoperative day when pancreatic juice was evacuated from her wound. A fistula developed which drained about 600 cubic centimeters a day, but this gradually diminished until she had a daily amount of about 50 cubic centimeters coming from a small sinus in the wound. This complication was attributed to the difficulty in closing the thin neck of the pancreas. She had episodes of chills and fever between periods of normal temperature for which no adequate explanation could be found in spite of diligent study. She was kept in the hospital for this but she became so desirous of returning to her home that she was finally discharged on her 58th postoperative day. Final diagnosis was carcinoma of the duodenum.

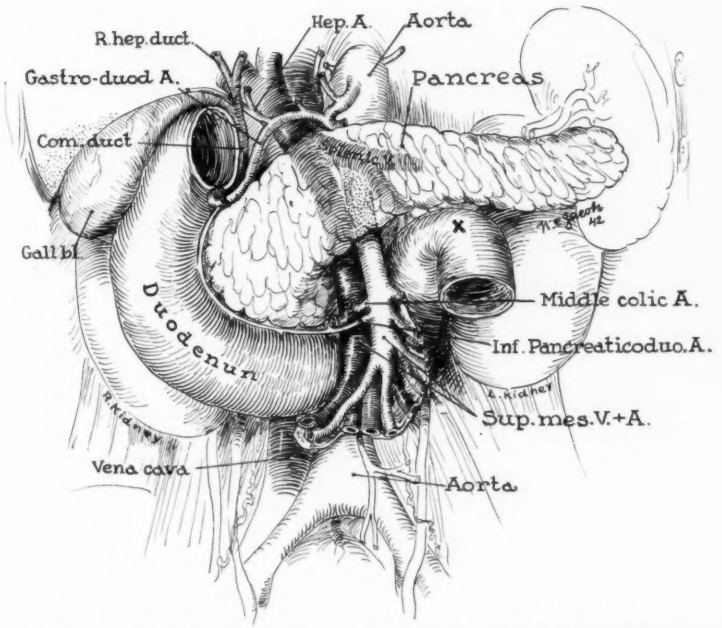


Fig. 2. The anatomy of the dissection is shown. When Treitz's ligament is cut and the vessels supplying the fourth part of the duodenum are ligated, the bowel will slip under the superior mesenteric and middle colic vessels. It is easy to do this if the inferior pancreaticoduodenal artery is first ligated and these vessels are lifted up off the duodenum with a retractor. This also assists in exposing the uncinate process of the pancreas. The bowel is divided at *X* and the distal portion brought up to anastomose with the gall bladder. The pancreas is divided just in front of the superior mesenteric vein.

Soon after this 7 hour operation was started, a cannula was placed in a branch of the great saphenous vein from which blood samples were frequently taken and into which parental fluid and blood were given. This method has been used by Mahoney and allows periodic determination of the hematocrit, specific gravity, and plasma protein. It permits the intelligent administration of saline, plasma, or whole blood and so gives the surgeon assurance of the condition of his patient during such long operations.

The anastomosis here described is only applicable if done in one stage when the entire duodenum is removed. Several cadavers have been studied and in all it was possible to roll the duodenum out from beneath the superior mesenteric vessels. Before this can be done Treitz's ligament must be cut and in some subjects the vessels to the fourth part of the duodenum must be ligated and divided. However, then the mesentery of the jejunum is long enough to bring the bowel to the gall bladder without tension, for this is a shorter distance than in most antecolic anastomoses.

There is advantage in the antiperistaltic attachment of the bowel to the biliary tract, for it offers the best chance of avoiding ascending biliary infection. The operation described would appear to be the simplest way to do this, avoiding as it does the complicated Roux anastomosis. It would seem that the end-to-side gastrojejunostomy is as good as the posterior side-to-side gastroenterostomy and it is much easier to do, for the structures are clearly exposed. It should be placed at least 6 inches from the gall-bladder suture to avoid reflux into that organ.

It might be argued that resection of the entire duodenum is unnecessary and prolongs the operation, but actually it is not hard to do and takes very little time once the anatomy is visualized. It has the advantage of giving a clearer view of the portal vein and pancreas than is obtained in any other way which facilitates the dissection of a region that is difficult to expose under other circumstances.

The resection of the duodenum and head of the pancreas in one stage is applicable only in "good

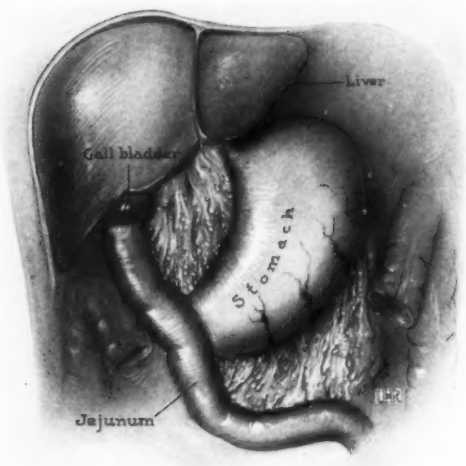


Fig. 3. This drawing illustrates the relation of the viscera at the end of the operation. Probably more jejunum than is shown should be left between the gall bladder and the stomach to prevent any reflux of gastric contents into the biliary tract.

risk" cases. It is much easier and safer to do the dissection in a clean field free from adhesions where the normal anatomical relations are undisturbed. Moreover there is no interference by anastomoses which frequently get in the way during the second stage of resection. But in spite of this, in the presence of debility, cachexia, or severe jaundice, it is safer to divide the operative burden into two stages. This may be illustrated by a personal experience. It happened that the day after the operation described an exploratory operation was done on another patient with carcinoma of the ampulla of Vater. Here the growth was small, there were no glands, but there was intense, long standing jaundice. Naturally, it was desired to repeat the simplified one stage resection, but the patient tolerated operation poorly, and it was evident that a two stage procedure was preferable so the typical operation of Whipple was done. Even the enthusiasm for a new operative technique could not blind one to the obvious advantages of the two stage operation under these circumstances!

SUMMARY

A method of one stage resection of the duodenum and head of the pancreas is described which restores the continuity of the biliary and digestive tracts with only two anastomoses. This technique retains the advantage of an antiperistaltic intestinal biliary union but in a simplified form.

REFERENCES

1. Brunschwig, A. Surg. Gyn. Obst., 1937, 65: 681.
2. Coffey, R. C. Am. Surg., 1909, 50: 1238.
3. Halsted, W. S. Boston M. & S. J., 1899, 141: 645.
4. Horsley, J. S. Ann. Surg., 1941, 113: 802.
5. Hunt, V. C. Ann. Surg., 1941, 114: 570.
6. Lahey, F. H. Surg. Gyn. Obst., 1933, 57: 227.
7. Mahoney, E. B., Kingsley, H. D., and Howland, J. W. Ann. Surg., 1941, 113: 969.
8. Mall, F. Johns Hopkins Hosp. Rep., 1896, 1: 93.
9. Mann, F. C., and Bollman, J. K. Ann. Surg., 1931, 93: 794.
10. Mayo, W. J. Ann. Surg., 1906, 44: 209.
11. Moynihan, B. Abdominal Operations. Vol. 2, p. 426. Philadelphia: W. B. Saunders Co., 1914.
12. Sauve, L. Rev. chir., 1908, 37: 335.
13. Trimble, I. R., Parsons, J. W., and Sherman, C. P. Surg. Gyn. Obst., 1941, 73: 711.
14. Whipple, A. O. Am. J. Surg., 1938, 40: 260.
15. Whipple, A. O., Parsons, W. B., and Mullins, C. R. Ann. Surg., 1935, 102: 763.

# TENDON TRANSPLANTATION OF THE FLEXOR CARPI ULNARIS FOR PRONATION-FLEXION DEFORMITY OF THE WRIST

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THE functional capacity of the hand is largely dependent upon the ability to extend the wrist and supinate the forearm. If the wrist is in the flexed position, the hand has a very poor grasp and is generally ineffectual. Weakness of the extensor muscles of the wrist and a combined deformity of wrist-flexion and pronation are common in spastic, obstetrical, and infantile paralysis. Any procedure which will correct this abnormal position and allow active extension and supination greatly improves the function of the hand.

Transplantation of the tendon of the flexor carpi ulnaris into the tendon of the extensor carpi radialis longus is an effective procedure in correcting this deformity. It is particularly indicated to aid active extension of the wrist but, since the transplanted muscle is directed around the medial margin of the ulna to be inserted into the radial side of the hand, it is helpful in promoting active supination. The operation has been equally applicable in chosen cases of the three types of paralysis mentioned, and may be indicated in the residual deformity arising from a lesion of the radial nerve.

The criteria and indications for the procedure vary depending upon the original paralytic lesion. Before the operation is contemplated, it should be established that the flexor carpi ulnaris is of "normal" or "good" power; a transplant involving a "fair" or "poor" muscle cannot be expected to function. It is necessary, likewise, that the other musculature affecting the hand should be of sufficient quality to allow satisfactory function after the transplant.

Since a transplanted muscle will not function effectively if it is handicapped by a deformed position, it is essential that the deformity should be correctable passively, at least after the flexor carpi ulnaris is divided. If the deformity cannot be corrected passively, it may be necessary to carry out accessory procedures to allow such correction, either preliminary to or at the time of the transplant. On occasion it has been necessary to divide the tendon of the pronator teres at its insertion, transplanting it from the dorsolateral surface to the volar surface of the radius, and in one case, this was combined with a stripping of a part of the interosseous membrane at its attachment to the radius. Although it has not been necessary in this series, it is likely that osteotomy of the radius and ulna immediately proximal to the wrist joint with or without excision of a small part of the shaft may be desirable as a preliminary procedure to correct the flexion of the wrist in more resistant cases. It is rare that such accessory procedures are indicated in spastic paralysis.

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## TECHNIQUE OF OPERATIVE PROCEDURE

The procedure is best carried out, provided the elbow can be extended, with the patient lying in the prone position with the arm abducted at a right angle on an arm board. A longitudinal incision, approximately 2 inches long, is made on the volar surface of the forearm, extending from the pisiform bone upward along the course of the flexor carpi ulnaris tendon. The distal end of the incision should be just proximal to the transverse skin line of the wrist. The tendon is isolated and severed at its attachment to the pisiform. The end of the tendon is grasped with an Allis clamp and freed as far proximally as possible through this incision. The ulnar nerve and vessel may be recognized beneath the tendon (Fig. 1). A silk suture of No. 2 braided silk is then introduced into the end of the severed tendon in *X* fashion.

A second incision, approximately 3.5 inches long, is made over the medial aspect of the forearm over the belly of the flexor carpi ulnaris muscle (Fig. 2). This incision should start approximately 2 inches below the medial epicondyle, and is directed distally and dorsally so as to expose not only the belly of the muscle but also the medial edge of the dorsal compartment of the forearm. When the deep fascia is uncovered, the margins of the flexor carpi ulnaris may be defined by traction on the tendon from the distal incision. An incision is then made through the deep fascia over the muscle. The dissection is carried be-

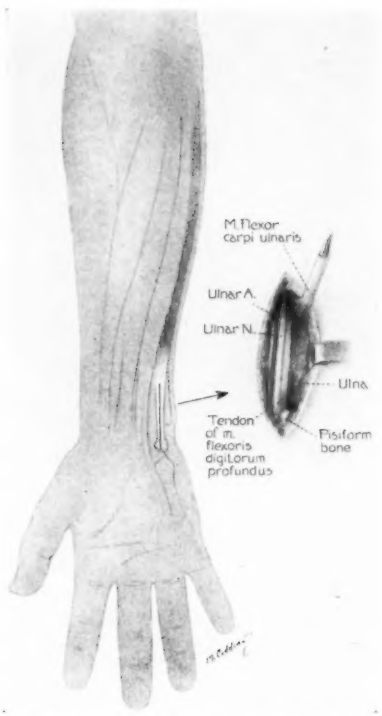


Fig. 1. The first incision over distal end of flexor carpi ulnaris at insertion into pisiform bone is shown. In inset the tendon is divided and retracted, exposing ulnar nerve.

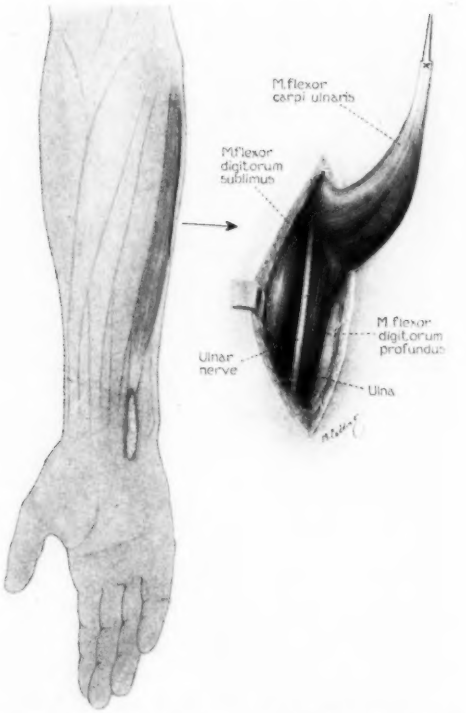


Fig. 2. The site of the second incision may be seen. The inserted drawing shows the tendon drawn into this incision, and the muscle freed in a proximal direction.

neath the muscle distally toward the first incision, freeing its attachment to the ulna in this region as completely as possible.

The silk suture, previously introduced into the tendon, is carried from the distal to the proximal incision by means of a tendon passer, and the tendon is drawn into the proximal incision. On occasion, since the ulnaris muscle is attached almost the full distance of the ulna, secondary dissection may be necessary. The short muscle fibers attached to the ulna in the distal portion are sacrificed, as indicated.

The muscle is freed by dissection in a proximal direction so that a straight line may be developed from its origin to its intended insertion into the extensor carpi radialis longus (Fig. 2). The nerve to the muscle must be preserved, but since it enters the muscle in its proximal portion, this is easily accomplished. Through this same incision, the medial dorsal margin of the ulna is recognized. Incision is made through the fascia over the extensor carpi ulnaris muscle, and the dorsal compartment of the forearm is entered (Fig. 3). The periosteum should not be exposed, and the opening into the dorsal compartment should be sufficiently large to allow free entrance of the muscle.

A third incision, approximately 2 inches long, is then made over the course of the extensor carpi radialis longus just above the wrist joint (Fig. 3). The tendon of the extensor carpi radialis longus is recognized and isolated. A tendon passer is then introduced from the proximal incision through the previously prepared opening into the dorsal compartment and delivered down to the third and final incision along the course of the extensor digitorum communis (Fig. 3). It is brought out adjacent to the extensor carpi radialis longus tendon. The distal end of the flexor carpi ulnaris is then drawn down into the dorsal incision, with care to assure that the muscle and tendon are in no way constricted. The course of the muscle should be essentially a straight line from its origin to the prospective insertion, when the forearm is in supination.

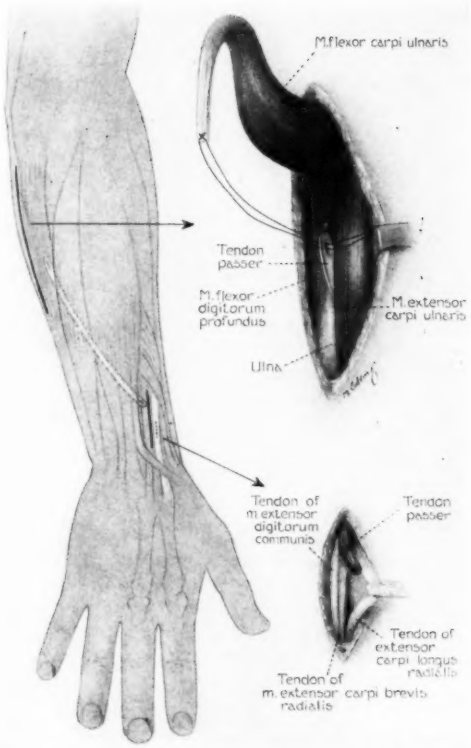
M. flexor carpi ulnaris
Tendon passer
M. flexor digitorum profundus
M. extensor carpi ulnaris
Ulna
Tendon of m. extensor digitorum communis
Tendon passer
Tendon of extensor carpi longus radialis
Tendon of m. extensor carpi brevis radialis

Fig. 3. The third incision exposing tendon of the extensor carpi radialis longus is illustrated. The upper inset shows the tendon passer entering the dorsal compartment of the forearm. Below, the distal end of the passer may be seen coming out alongside the extensor carpi radialis longus.

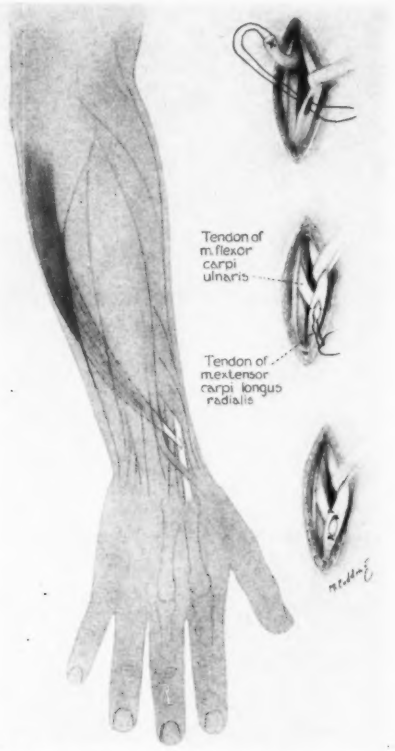


Fig. 4. The transplanted muscle is now in position. The method of insertion into the extensor carpi radialis longus may be seen.

The tendon of the extensor carpi radialis longus is incised and the ulnaris tendon is then sutured into it, with the forearm in supination and the wrist in dorsiflexion (Fig. 4). The tension of the transplanted tendon should be moderate, but it should hold the hand in the corrected position. The arm is immobilized in a bivalved plaster splint from the metacarpophalangeal joints to a point just below the axilla, with the elbow flexed at a right angle, the forearm in complete supination, and the hand in dorsiflexion.

Ordinarily, guided active exercises are started on the third day following operation. The result from the transplant may well depend upon the efficiency of the physiotherapeutic regimen. The training of the muscle to carry out its new function is best accomplished by having the patient attempt ulnar deviation of the wrist as the hand is carried into dorsiflexion and supination, an exercise which combines the new function with the old. The hand is held in the corrected position by the bivalved plaster splint for a variable period of time, as indicated. Often a night splint is used for a long period, particularly in cases of cerebral palsy. Removal of the support too early may defeat the function of the transplant, as may cessation of physiotherapy before the transplant is effective.

### SPASTIC PARALYSIS

In spastic paralysis involving the upper extremity, the hand is frequently in a position of flexion and ulnar deviation at the wrist, with the forearm in pronation. Attempts at extension and supination vary in their effectiveness. In many instances, there is utter inability to carry out these motions. In others, the function is performed in such incomplete fashion that it is ineffectual. Weakness of the extensor muscles of the wrist is usual.

Fig. 5. R. P., patient with spastic hemiplegia. a, left, Illustrates difficulty in active extension and supination. b, right, Postoperative status of patient 3 months later.

The flexor carpi ulnaris is often one of the major deforming elements in that it pulls the wrist into flexion and ulnar deviation. The transplant in these instances accomplishes its purpose in a two-fold fashion: division of the flexor carpi ulnaris removes it as a deforming factor; the transplantation of the tendon into the extensor carpi radialis longus increases the power of extension.

R. P., male, aged 9 years, was admitted to the Children's Hospital on April 1, 1940, with spastic hemiplegia, left.

Physical examination corroborated this diagnosis, which had been made previously. Voluntary motions of the left hand and wrist were difficult. Attempted use of the hand provoked increased spasticity with flexion and ulnar deviation of the wrist, pronation of the forearm, and hyperextension of the fingers. Active supination was to neutral only. Passively the parts could be carried through a full range of motion. The other upper extremity was entirely normal. Limitation of active supination and extension is shown in the preoperative photograph (Fig. 5a).

Transplantation of the flexor carpi ulnaris to the extensor carpi radialis longus was done on April 24, 1940. Examination of July 11, 1940, showed greatly improved function, as may be seen in the photograph taken at this time (Fig. 5b). Supination lacked only a few degrees of being equal to the other side, and active dorsiflexion of 45 degrees was present.

F. D., female, aged 9 years, 9 months, was admitted to the Children's Hospital on July 16, 1940, with the diagnosis of spastic hemiplegia, left. On a previous admission to the hospital, in May, 1934, a Stoeffel neurectomy of the branch of the median nerve to the pronator teres had been done. This had resulted in little or no improvement.

Examination of the left arm showed poor function in the left wrist with ulnar deviation, limited and weak active extension, and active supination only 30 degrees beyond neutral (Fig. 6a). Attempted dorsiflexion and supination were accompanied by many accessory motor activities.

On July 17, 1940, tendon transplantation of the flexor carpi ulnaris to the extensor carpi radialis longus was done.

Follow-up examination of March 17, 1941, showed excellent function of the hand in all respects, as may be seen (Fig. 6b). Supination was essentially complete. She had good active dorsiflexion with an excellent grip.

The transplant has been carried out in 15 cases of spastic paralysis. All of these have had an end-result determination varying from 1 to 8 years after the operation. In classifying the result, the criteria were necessarily different from those in a flaccid paralysis, and took into consideration the fundamental motor dysfunction.

Of the 15 cases, all have been improved. In 12, this improvement was recorded as marked, and in 3, moderate.

The operative result has been classified as "excellent" in 9; "good" in 4; "fair" in 1, and "poor" in 1. The one recorded as "poor" showed marked

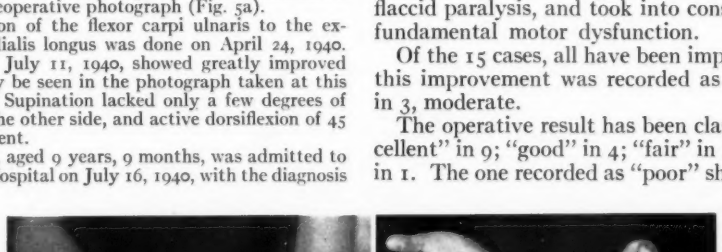

Fig. 6. F. C., patient with spastic hemiplegia. a, left, The limitation of active supination of the forearm and extension of the wrist on the left are shown. b, right, Same patient 8 months after tendon transplantation of flexor carpi ulnaris into extensor carpi radialis longus.

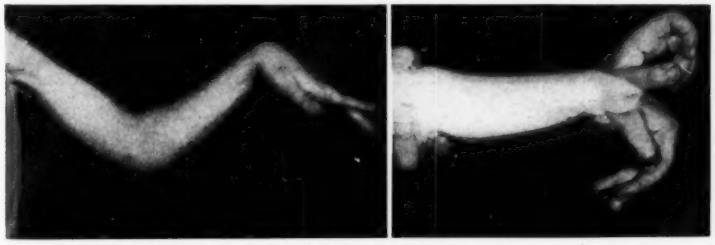

Fig. 7. B. C., patient with obstetrical paralysis. a, left, Photograph illustrates the maximal active dorsiflexion of the wrist. b, right, Same patient 6 years after operation. Phantom photograph illustrates range of active flexion and extension of wrist. Excellent function of hand.

spasticity with minimal control. In this case there was definite improvement in function from the procedure, but subsequently a fusion of the wrist was done with little further improvement. The patient recorded as having a "fair" result showed marked spasticity with minimal control, and was mentally retarded.

Of the 4 in the "good" group, 2 showed quite marked spasticity; 1 was mentally retarded; and the other showed excellent function of the transplant, but the capacities of the hand were limited by an adduction deformity of the thumb which had not yet been corrected.

In 2 of the patients, a neurectomy of the branch of the median nerve to the pronator teres had been done several years before with little effect. In 1 of these, it was our impression that the hand would have had better function if the preliminary neurectomy had not been done, since there was weakness in pronation after the transplant, which we associated with the previous operation. In 1 instance, a neurectomy was done at the same time as the transplant, and in this case the result was excellent.

In those cases in which the extensors of the fingers have been rated as "poor," it has been questioned whether the transplant should be inserted into the extensors of the fingers, or into the extensor of the wrist. Usually the choice has been to place the transplant into the wrist extensor, and, subsequently, with the wrist in the improved position and with muscle training, the extension of the fingers has been very satisfactory. In a few cases not included in this series, the transplant has been inserted into the finger extensors with satisfactory result.

Adduction of the thumb is quite a common deformity in spastic paralysis. Often with the improved position of the hand following the operation and with muscle training, further procedures are not necessary. An adequate trial should be given after the operation before an operative procedure on the thumb is performed.

The transplant is least effective when the spasticity is very marked and the patient has little active control of the hand. It is not indicated in the presence of gross mental deficiency.

### OBSTETRICAL PARALYSIS

In obstetrical paralysis of the "whole arm" type with partial recovery of the hand, the extensors of the wrist may be the only muscles which do not have a return of power. It is in these instances that the operation is particularly indicated, although it may be helpful in other cases in which the residual paralysis is more extensive.

B. C., female, aged 11 years, 10 months, was admitted to the Children's Hospital September 5, 1934, because of functional incapacity of the left arm dating from birth. She had been admitted to this hospital on two previous occasions, and a diagnosis of obstetrical paralysis of "whole arm" type had been made. At one admission, on October 11, 1928, she had had a Sever procedure; that is, a division of the subscapularis and pectoralis major tendons, as well as the origin of the short head of the biceps and coracobrachialis muscles.

On physical examination, the child had marked disability of the left arm and hand (Fig. 7). The hand lacked 30 degrees of reaching the neutral position in active extension, although it could be passively extended to neutral. Active supination was limited to 20 degrees. The motion of the fingers was good, although their function was poor, due to the flexion-deformity of the wrist.

On September 8, 1934, the flexor carpi ulnaris tendon was transplanted into the extensor carpi radialis longus. The arm and forearm were held in the corrected position by a bivalved circular plaster splint. Physiotherapy was started 5 days after the operation.

Follow-up examination of June 26, 1940, almost 6 years later, showed 60 degrees of active extension of the wrist, with flexion of 30 degrees (Fig. 7). The hand at this time had excellent function in all respects, although there remained some limitation in supination.

This transplantation has been done on 6 cases of obstetrical paralysis, with improvement in all. The end-result was recorded as "excellent" or

a b c

Fig. 8. J. L., patient with anterior poliomyelitis. a, The photograph is poor but illustrates the absence of active dorsiflexion of wrist and the presence of "fixed pronation." b and c, Same patient 2 years after operation. Photographs illustrate the degree of active supination as well as range of active flexion and extension of wrist.

"good" in 4, "fair" in 1, and "poor" in 1. The patients in whom the "poor" and "fair" results were obtained had extensive paralysis affecting the forearm and hand and the transplanted muscle was recorded as not better than "fair plus" in power before the operation.

### ANTERIOR POLIOMYELITIS

In our series, the indication for this procedure in infantile paralysis has been less frequent than in spastic and obstetrical paralysis. It is a little unusual to have a "good" or "normal" flexor carpi ulnaris associated with paralysis of the extensors of the wrist, and yet with sufficient power in other muscles to allow improved function by this procedure. When indicated, it has been helpful indeed.

J. L., male, aged 14 years, 5 months, was admitted to the Peter Bent Brigham Hospital on October 28, 1938, with a complaint of disability of his right arm from anterior poliomyelitis, which he had developed in August, 1927.

On examination, there was a complete wrist-drop on the right with no active extension against gravity, and a marked pronation contracture, amounting to 45 degrees, with very little active supination.

Muscle examination of the forearm and hand showed the extensor carpi radialis and extensor carpi ulnaris to be rated "poor"; the finger extensors, biceps, and supinator brevis were "fair," and the triceps was "poor." The other muscles effecting the forearm and hand were "good" to "normal." The preoperative photograph is poor, but does suggest the function of the hand (Fig. 8a).

On October 28, 1938, transplantation of the flexor carpi ulnaris into the extensor carpi radialis was done. In addition, in order to relieve the pronation contracture, it was necessary to divide the pronator radii teres at its insertion on the dorsolateral aspect of the radius, and reattach it to the anterior surface of the radius after the hand had been supinated. The interosseous membrane was stripped from the radius over a part of its extent in order to decrease further the pronation contracture.

Follow-up examination of December 6, 1940, showed excellent dorsiflexion amounting to 60 degrees with almost complete active supination. His grasp, which previous to operation had been poor indeed, was excellent. Phantom photograph (Fig. 8c) shows the range of flexion and extension of the wrist.

The procedure has been performed in only 2 instances of infantile paralysis. The result in the case just presented must be rated as "excellent," and in the other case the result was "good."

### SUMMARY

1. The function of the hand is greatly impaired by a flexion-pronation deformity of the wrist, a condition which is common in spastic, obstetrical, and infantile paralysis.

2. Tendon transplantation of the flexor carpi ulnaris into the extensor carpi radialis longus is an effective procedure in correcting this deformity and in promoting active extension and supination in cases which satisfy certain preoperative criteria.

3. This transplant has been done in 23 instances: 15 were in spastic paralysis; 6 in obstetrical paralysis; and 2 in anterior poliomyelitis. The majority were greatly improved.

# REDUCTION OF THE PERMANENT PARTIAL DISABILITY OF COMMINUTED FRACTURES OF THE LOWER END OF THE RADIUS BY SKELETAL TRACTION

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COMMINUTED fractures of the lower end of the radius are serious. With the accepted treatment they consistently heal with a lamentable high percentage of permanent partial disability. This disability is the result of shortening of the radius with a radial deviation of the hand and resulting pain. In an attempt to remedy this situation we use a method of skeletal traction. In most instances we believe that we have overcome this disability.

Working from the premise that the lower end of the comminuted radius compressed upon itself because of muscle spasm, we felt that by overcoming the spasm the fragments would heal with the length of the radius unimpaired, and consequently the radial deviation of the hand and pain would not develop.

The banjo splint with direct or indirect traction going through the joints of the thumb has previously been proved unsatisfactory because of

a b

Fig 1. a, Comminuted fracture of the distal end of the radius; b, satisfactory result following conservative treatment after 4 months. Patient allowed 15 per cent permanent partial disability as compared to an amputation at the wrist.

a b c

Fig. 2. a, Comminuted fracture of the distal end of the radius. b, End-result after 6 weeks. Note restoration of length of radius and hole left by Kirschner wire in the first metacarpal bone. c, End-result after 7½ months. No permanent partial disability awarded.

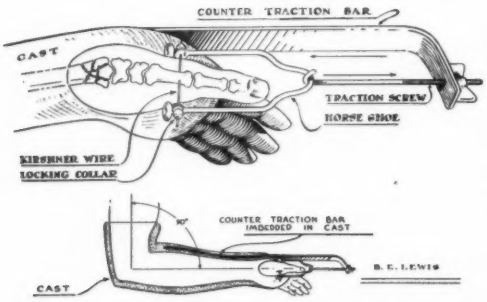


Fig 3. Schematic drawing showing method of applying traction. The cast is molded beneath the fracture with slight volar and strong ulnar deviation of the hand.

joint damage. However, skeletal traction through the first metacarpal seems to have the necessary requirements with the minimum of disagreeable points.

Under general or local anesthesia the fracture is reduced as much as possible by manipulation. With the hand in slight volar and strong ulnar deviation a circular cast from the metacarpophalangeal joints to above the elbow is applied. The cast is widely removed about the thumb. A Kirschner wire is then placed transversely through the distal end of the first metacarpal, care being taken to avoid the joint surfaces. A special horseshoe which allows free motion of the thumb is attached to the wire and held in place by two locking collars. Traction is applied by a threaded screw with countertraction being maintained by an L shaped bar imbedded in the cast (Fig. 3). The normal length of the radius can be maintained by exerting sufficient traction through the first metacarpal bone. Traction is maintained for 6 to 8 weeks, after which the future care is dependent upon the amount of healing. In no instances have we been required to maintain further traction. It can be seen that the convalescent period is slightly prolonged, but we feel that our results justify the means. The morbidity otherwise is not increased.

Figures 1a and 1b show the usual result following the accepted method of treatment while Figures 2a, 2b, and 2c show a typical case following the use of bone traction.

# A MODIFICATION OF THE HIGGINS TECHNIQUE FOR URETEROINTESTINAL ANASTOMOSIS

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IMPLANTATION of the ureters into the bowel presented a problem which all but defeated the earlier operators. The present status of relative success is attributable to the genius of Coffey, who 30 years ago, developed the technique of oblique submucosal implantation based on the valve principle. The obvious advantages of this procedure stimulated new interest and made ureterointestinal anastomosis justifiable. With increasing experience based on more than a thousand such operations, this procedure has become firmly established and its application has been extended beyond cases of exstrophy and carcinoma of the bladder to include epispadias, tuberculous cystitis, Hunner ulcer, vesicovaginal fistula, and similar conditions. Maximum results are achieved by operative intervention, before the ureters are dilated and the kidneys damaged by infection. The simpler surgical procedures involving minimal trauma to the ureter and intestine are recognized as best.

The first two of Coffey's methods are more frequently employed than any other. The results are fairly satisfactory, but the limitations to a unilateral anastomosis with the first and the inapplicability to ureters smaller than No. 10F plus the complicated equipment and postoperative care necessary for the second are decided disadvantages. To these must be added the likelihood of the development of urinary sepsis. More than 60 techniques have been advocated for the correction of these conditions. Many are based on lateral anastomosis of the ureter and the mucosa of the bowel with immediate or subsequent formation of a fistulous opening. Ingenious methods and special electrocoagulation devices have been utilized for this purpose. It seemed to us, at least in theory, that a satisfactory fistulous opening would be more likely to result from properly and accurately placed sutures than from the secondary use of electric cutting devices, provided the technique insured the immediate and continued adequacy of the stoma.

In 1933 Higgins first published a description of his principle of the "intact ureter" operation. His work as well as that of Coffey and others proved that a fistula can be established between the ureter and the colon without opening into the intestinal lumen. The advantage of the Higgins procedure is that one stage bilateral implantation without interruption of urinary excretion is feasible. The advantages over the two stage operation are obvious and in cancer may be life-saving. The possibility of delayed, partial or complete occlusion of the fistulous stoma has operated to prevent the more general adoption of this procedure. An instance from our experience, illustrative of this, involved a child who was successfully operated upon by the Higgins technique for congenital absence of the bladder neck. During the following 3 years, gradually increasing dilatation of the ureters and pelvis was observed, and death resulted from bilateral stenosis at the sites of implantation.

With the object of obtaining a more widely patent and permanent fistulous opening, a series of studies involving the placement of the necrosing sutures was carried out. It was ultimately observed that single sutures introduced either transversely or longitudinally in the ureter produced fistulas which were not as satisfactory as those resulting from crucially placed ones. To secure the advantage accruing from cruciform sutures, the following technique was developed.

A small rubber catheter with terminal and lateral eyes is prepared in advance by suturing a few thicknesses of vaseline gauze to the shaft for a short distance proximal to the lateral eye. When induction of anesthesia is complete, this catheter is introduced into the rectum. After the usual skin preparation, the exstrophic area is isolated from the field by a sheet of sterile rubber dam, the upper margin of which is secured to the skin with skin clips and collodion. The patient is placed in the Trendelenburg position, a midline incision is carried through the peritoneum, and extended the full length of the wound. The intestines are displaced upward and supported with moist laparotomy pads.

The right ureter (Fig. 1) identified through the peritoneum as it courses downward over the sacral notch, is exposed by sharp dissection and mobilized for approximately 2 inches. A site in

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Read before the Genito-Urinary Section, New York Academy of Medicine, November 18, 1941.

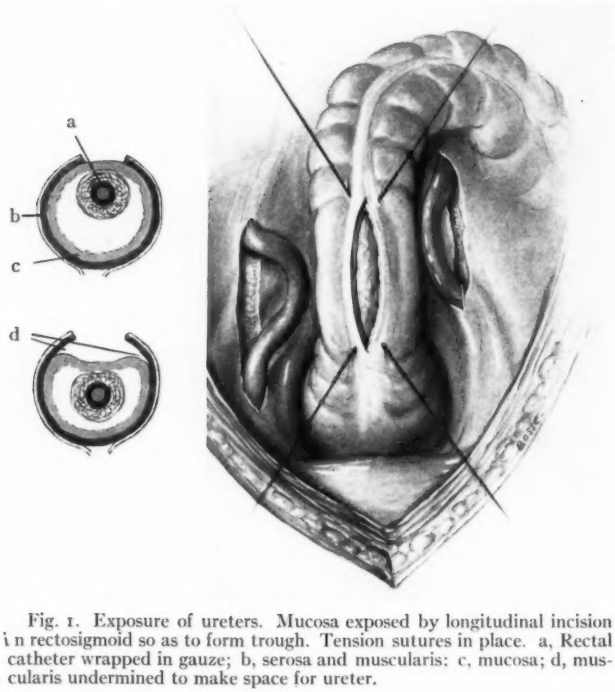
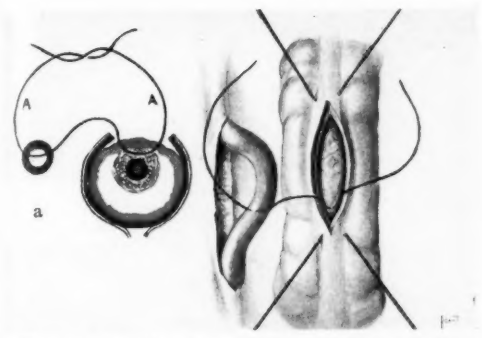



Fig. 1. Exposure of ureters. Mucosa exposed by longitudinal incision in rectosigmoid so as to form trough. Tension sutures in place. a, Rectal catheter wrapped in gauze; b, serosa and muscularis; c, mucosa; d, muscularis undermined to make space for ureter.

the rectosigmoid, adjacent to the exposed ureter, is selected and 4 silk traction sutures are placed, 2 on either side of the linea alba, one pair 2 inches above the other. While moderate traction is exerted on these sutures and the bowel wall is stretched over the tube, a 1½ inch longitudinal incision is made through the serosa and muscularis to the mucosa. The superficial layers are next undermined to form a trough, the mucosa being left intact. One should bear in mind Coffey's warning that damage to the vessels in this structure may result in sloughing of the mucous layer.

The ureter (Fig. 2) is placed in the trough and steadied by the traction sutures in such a manner that kinking and tension are avoided. A silk suture is then passed transversely through the lumen of the ureter, and through the mucosa of the rectosigmoid including in its bite, the gauze around the rectal tube before it emerges. It is best placed at the lower angle of the intestinal incision. A similar suture is placed in the long axis of the ureter at right angles to the first, through the lumen of the ureter, the mucous membrane of the bowel, and the gauze. The second suture is looped through the first and both are tightly tied. Thus not only are the ureter and sigmoid doubly anchored, but the resulting necrosis as the sutures cut through provides a relatively large fistula, quadrilateral in shape (Figs. 3 and 4). The muscular and serous layers are approximated over the ureter by interrupted silk sutures and the lateral tension sutures are used as a reinforcement. The wound in the bowel is partially extraperitonealized by suture of the outer edge of the posterior peritoneum to the intestinal wall. We have not found complete extraperitonealization essential; since limited motility of the bowel is desirable as Lower has stated. After a similar procedure is carried out on the left side, sulfathiazole powder is freely dusted on the peritoneal surfaces and the anastomosed areas. The abdominal wound is closed in layers; tension sutures are inserted, no drainage is used.

Attempts to eradicate renal infection, if present, and improve renal function should be carried out as part of the preoperative preparation. The sulfonamide drugs are well tolerated by these patients and their administration in more recent cases before and during the operative period has been helpful. The postoperative course, in the absence of extraurinary complications, is usually uneventful. Fluids are withheld by mouth for 24



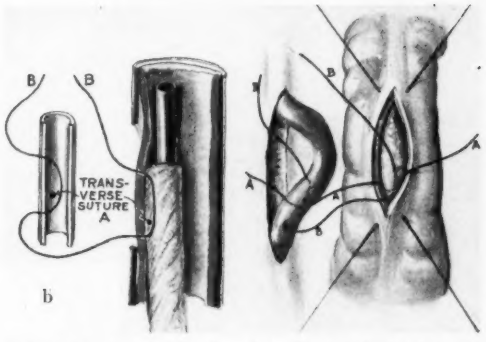




Fig. 2. a, Insertion of transverse suture through ureteral wall, mucosa of bowel, including in its bite gauze covering rectal tube. b, Introduction of similar longitudinal suture at a right angle to first.

hours but freely administered by clysis and intravenous drip. The rectal tube is kept open by frequent small injections of normal saline solution and comes away, as a rule, within a week. In the interim, excretion from the ureteral orifices is variable but has been adequate. After the exit of the rectal tube, drainage from the bladder diminishes considerably. In some individuals the exstrophic area has been practically dry at the end of a few weeks, thus indicating the establishment of adequately patent fistulas. The resulting absence of soiling facilitates nursing care, and permits delaying the removal of the bladder in the event that this step must be deferred. Thus, the time for cystectomy becomes optional rather than imperative. Successive postoperative urographic studies have demonstrated that the immediate dilatation of the ureters and pelves following neostomy gradually diminishes during the first few months, and even over longer periods of time.

CASE 1. A.D., a 2 year, 9 month old male, was admitted to our hospital on April 14, 1939, with congenital exstrophy of the bladder and an unexplained anemia. The urine on microscopic examination showed a trace of protein and 10 white blood cells and an occasional clump per field. The blood count revealed a marked secondary anemia. Chemical blood studies showed values at the upper limits of normal. Urography showed a separation of the symphysis pubis, rotation of the left kidney, and tortuous ureters with dilated lower portions.

He was sent home for tonic treatment in an effort to improve his general condition and was returned June 10, 1940,

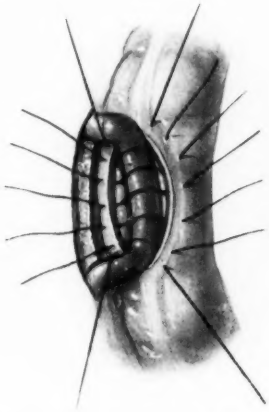


Fig. 3. Ureter in trough with crucially placed sutures tied tightly. Sutures for embedding ureter in place.

Fig. 4. Bilateral implantation of ureters with muscularis sutured. Peritoneal edge to be sutured to bowel.

Fig. 5. Case A. D. Intravenous urogram before operation. Note rotation of left kidney.

Fig. 6. Case A. D. Intravenous urogram 17 months after ureteral implantation.

at which time there was no appreciable morphological change in the urograms though the contrast medium appeared in slightly greater concentration (Fig. 5). Ten days later bilateral implantation of the ureters into the sigmoid was carried out with the use of crucially placed sutures. His immediate postoperative condition was fair. Chemical blood studies showed a rise of urea nitrogen from 34.5 the day after operation to 52.5 on the second day. On the 4th day it was 49.0. Thereafter it dropped gradually reaching 21.0 on the 6th postoperative day when the rectal tube came away, and remained slightly elevated for a month. The excretion from the ureteral orifices in the bladder continued to decrease. Twenty-five days after neostomy intravenous urography revealed slight dilatation of the right kidney pelvis and calices; moderate dilatation of the left pelvis and calices; moderate dilatation of both ureters with good concentration in the sigmoid.

The child was readmitted for cystectomy 2 months after the implantation. The postoperative stay was prolonged by delayed healing of the wound. An intravenous urogram, 3 months later, revealed the right kidney pelvis to be slightly dilated with further blunting of the minor calices. The left kidney was rotated, its pelvis moderately dilated, with increased dilatation and blunting of the calices. The left ureter was considerably dilated and displaced to the left. Contrast medium was seen in the distal sigmoid and the rectum.

The patient, on discharge, was in good condition. A recent intravenous urogram, 17 months after the ureteral implantation (Fig. 6), shows the right ureter and pelvis to be almost normal. On the left side, there is less dilatation than on the previous examination.

Case 2. F. R., a 4 year old male with exstrophy of the bladder, was admitted to the hospital on May 6, 1941, for implantation of the ureters into the sigmoid. The laboratory findings were as follows: urinalysis showed urine to be hazy, straw, alkaline, 1 to 2 red blood cells per high power field, 12 to 18 white blood cells per high power field with many clumps, 4 plus acetone. Chemical examination of the blood showed no abnormality. Intravenous urograms revealed congenital maldevelopment of the pubic bones. The pelvic portions of the ureters were deflected laterally.

On May 10, 1941 a bilateral implantation of the ureters into the bowel by the crucial suture method was performed.

Chemical blood studies showed an elevation of the urea nitrogen to 33.0 on the second postoperative day with a gradual reduction to normal on the ninth day.

On the 26th day after operation, an intravenous urogram revealed good function of both ureters with moderate dilatation of the right renal pelvis and dilatation and blunting of the calices of both kidneys. The child was discharged 31 days after implantation with only slight excretion from the ureteral orifices. He was readmitted for cystectomy 65 days after the implantation, the bladder having been dry for some time. Convalescence was uneventful and he was discharged on the 55th day after removal of the bladder. An intravenous urogram made just before his leaving showed marked reduction in lumen of the left ureter, the left kidney pelvis and calices, with a decrease on the right side.

The intravenous urographic studies in this case again demonstrate the progressive improvement

Fig. 7. Case 4, D. G. Intravenous urogram after implantation of right ureter. Right kidney functionless, left shows advanced hydronephrosis.

Fig. 8. D. G. Intravenous urogram after implantation of left ureter. Right side functionless, left shows recession of hydronephrosis.

of the ureters and pelvis for the first few months following implantation. Previous infection may have been a factor in the dilatation noted in the first series after operation.

Case 3. W. M., a male child, 3½ years old, was admitted on June 16, 1941, with exstrophy of the bladder. At this time intravenous urographic studies revealed faulty development of the pubic bones and normal morphology of the upper urinary tract. Due to an upper respiratory tract infection, operation was deferred to July 1, 1941, when anastomosis was carried out on the right ureter by the method described. The operation was terminated at this point because of the child's general condition. Convalescence was uninterrupted. Two weeks later, in implanting the left ureter, the mucosa was inadvertently incised while making the trough, due to distortion of the sigmoid by the first operation. The repair created an angulation of the ureter which apparently interfered with its patency. For several days following operation there was a rise of temperature without evidence of peritonitis. Small doses of sulfathiazole relieved the symptoms. An intravenous urogram 2 weeks later showed the presence of contrast medium in the right urinary tract at the end of 5 minutes with fairly normal morphology on this side. The medium was discernible on the left side at 15 minutes, increasing in concentration on later exposures. There was marked dilatation and blunting of the calices on this side. Cystectomy was deferred to a later date, and the patient was discharged from the hospital with no leakage from the right ureteral orifice and only a slight amount from the left. At this time intravenous urograms indicated adequate excretion into the sigmoid. This case illustrates the oft repeated dictum that implantation must be precise and technical errors may prove disastrous.

Case 4. D. G., a female child, was admitted to the Jersey City Medical Center on February 27, 1941, with a diagnosis of exstrophy of the bladder. On physical examination, the patient appeared chronically ill. Laboratory findings were as follows: urine negative but for occasional white blood cells on microscopic examination. Blood count revealed a secondary anemia.

On March 7, 1941, the right ureter was implanted into the lower bowel extraperitoneally by the attending urologist. Immediate postoperative condition was fair. Nine days after operation patient developed a fecal fistula which eventually closed. About 1 month later she contracted chicken pox and shortly afterward measles, but these two conditions subsided. Examination of the wound at this time revealed a large ventral hernia. On the 56th postoperative day an intravenous urogram (Fig. 7) revealed an advanced hydronephrosis on the left side, and failure of excretion on the right. At this time the general condition of the patient was fairly good and continued to improve until 3 months later, when a left ureterosigmoidneostomy

was performed, using crucially placed sutures. Convalescence proceeded without complication. On the 5th postoperative day the rectal tube came away, the feces became watery, and it was noted that very little urine was excreted from the ureteral orifices. The patient was discharged on her 25th postoperative day to be readmitted later for excision of the bladder. Two months later urograms (Fig. 8) showed good function with a marked decrease in the hydronephrosis on the left side, with complete lack of visualization on the right.

This case illustrates that a grossly dilated ureter may improve after implantation.

Experience with this method has shown that it fulfills the essential requirements of lateral anastomosis. It is relatively simple, and both sides may be done at one sitting without interruption of the flow of urine along the ureter during the period of formation of the fistula. The caliber of the fistulous opening is not limited to that of the lumen of the ureter; because the longitudinal sutures increase the aperture to an adequate size. We agree with Higgins, Lower, and others that operative intervention in infancy is better than indefinite delay with the resultant development of obstructive uropathy and infection. Sulfathiazole and other chemotherapeutic remedies, administered orally and applied locally at the operative site, have proved of inestimable value and recent reports of the efficacy of sulfaguanidine and allied agents as intestinal antiseptics indicate that they should prove a valuable supplement to our present preoperative and postoperative care. Our immediate results have been favorable. We hope that time and experience will demonstrate that the eventual outcome of these cases will be equally satisfactory.

## CONCLUSIONS

1. A modification of the Higgins technique is presented.
2. The use of 2 crucially placed sutures forms the fistulous opening between the lumen of the ureter and the sigmoid.
3. The resulting stoma is larger than can be obtained by single suture method.
4. There is no apparent loss of the valvular action of the mucosa.
5. The marked diminution in amount of leakage from the ureteral orifices as soon as the stoma is formed indicates that the fistulas are of adequate size.
6. The resultant absence of soiling makes the time of removal of the bladder optional.

## REFERENCES

1. Coffey, R. C. J. Am. M. Ass., 1911, 56: 397–403.
2. Idem. Surg. Gyn. Obst., 1927, 45: 816–819.
3. Idem. Northwest M., 1930, 29: 128.
4. Idem. Brit. J. Urol., 1931, 3: 353–428.
5. Idem. Northwest M., 1933, 32: 31–34.
6. Farrell, J. J., and Lyman, Y. Surg. Gyn. Obst., 1938, 66: 657–662.
7. Foley, F. E. B. Minnesota Med., 1937, 20: 65–67.
8. Higgins, C. C. Surg. Gyn. Obst., 1933, 57: 359–361.
9. Idem. J. Urol., Balt., 1937, 37: 90–105.
10. Hinman, F., and Weyrauch, J. M. Jr. Tr. Am. Ass. Genitourin. Surgeons, 1936, 29: 15–178.
11. Jewett, H. J. J. Urol., Balt., 1940, 44: 223–226.
12. Kerwin, T. J. Am. J. Surg., 1934, 23: 14–29.

# PRIMARY ADAMANTINOMA OF THE ULNA

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PRIMARY adamantinoma of the long bones is an extremely rare entity. Rankin, in 1939, reported the eleventh case of this tumor arising in the tibia. We believe the case of adamantinoma of the ulna recorded here is the first reported instance of the occurrence of this tumor in a long bone other than the tibia.

Adamantinoma or adamantine epithelioma is an infiltrating epithelial tumor, arising from basal cells, which grows in a stroma of fibrous tissue, and reproduces, to a certain extent, the histological characteristics of the primitive tooth bud. In the jaws it is a relatively common tumor. Cases have also been reported of this growth's arising in Rathke's pouch and invading the sphenoid bone.

Theories of origin are interesting, even if of little practical importance. In the jaws and in Rathke's pouch, this tumor probably arises from undifferentiated blocks of basal epithelium which developmentally, normally invaginate the underlying mesenchyma and preosseous tissue. In the long bones, the situation is quite different, and two theories have been advanced to explain the origin of primary adamantinoma in these bones. Fischer assumed the origin of such tumors to be in cell rests. This was based upon his belief that if the tumor cells were implanted at a time later than the fetal period, the potentiality to differentiate into tooth-like structures would not be present, and that pavement epithelium would result.

Ryrie, on the other hand, believes that the tumors arise from basal cells implanted in the deeper structures at the time of an injury. Even if the skin is unbroken, the deeper tissues and skin appendages, such as hair follicles, are torn, and implantation could result. It is interesting to note that in all of the reported cases, the patient recalled a severe blow to the long bone at the site of the ultimate tumor. This theory would seem to be further substantiated by the occurrence of adamantinoma in superficial long bones where the skin is closely apposed to the periosteum and where trauma is frequent. Our own feeling is that the theory of implantation is probably correct, and we suggest that perhaps the environment, i.e., bone, in which the basal cells are implanted is the determining factor in their differentiation into an adamantine tumor. This would seem to afford the opportunity for some enlightening experimental work in the fields of animal research and tissue culture.

Pathologically, the tumor is a soft, spongy, grey, indistinctly lobulated, vascular growth which occupies the central portion of the shaft of the bone and expands it without breaking through the cortex. Microscopically it is an infiltrating epithelial tumor in a stroma of fibrous tissue.

The epithelial elements are derived from a basal type of cell and may approach either squamous epithelium or enamel epithelium. These cells are arranged in tongue shaped or branching pseudoacinar processes which contain two distinct cell types, both of epithelial origin. The peripheral cells are of the cuboidal or tall columnar type, arranged in one or more layers with their long axes perpendicular to the limiting membrane of the cell group. These are comparable to the ameloblasts of the tooth bud. The central cells are of a cuboidal or transitional type with branching and anastomosing cytoplasmic processes which give a definite stellate appearance. This tissue represents the primitive enamel pulp. Cystic spaces are commonly present in the central area of the aggregations of cells. These may arise as a result of degeneration of the centrally placed stellate cells, so that the spaces are often filled with an amorphous coagulum and cellular débris.

The stroma is made up of fibrous tissue of varying degrees of density. Multinucleated giant cells are frequently present and may represent osteoclasts. A few inflammatory elements are sometimes found.

Clinically, adamantinoma of the long bones exhibits the following characteristics: Being a basal cell tumor, it possesses a limited type of malignancy. Once it is established in a bone, it may erode it to a considerable extent, but does not have the ability to invade adjacent tissues or to metastasize. Cases which recur after incomplete removal may involve surrounding structures. Either males or females may develop the tumor. The age incidence in reported cases is from 22 to 46 years. The chronicity and slow growth of the tumor are noteworthy; the time

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This work was supported by the Florence Hellman Ehrman Donation for Crippled Children and Research.

Fig. 1a.

Fig. 1b.

Fig. 1. Roentgenograms of the forearm taken on September 23, 1929, showing the tumor involving the shaft of the ulna.

Fig. 2.

Fig. 2. Roentgenograms, March 8, 1930, 3 months after partial resection of the ulna and implantation of a tibial bone graft.

elapsing between discovery of the tumor and surgical treatment in the reported cases has varied from 10 months to 16 years with the occurrence of only local extension. All patients give a definite history of trauma, usually not of sufficient severity to cause a fracture. Aching pain is often noted, but the usual presenting symptom is the presence of a tumor mass. Tenderness, increased local temperature, edema, and fluctuation may be present in some instances. There are usually no general symptoms such as are observed with malignant bone tumors. In spite of the relatively benign character of adamantinoma, it has a very strong tendency to recur if not completely removed. Treatment, therefore, consists in complete surgical excision, resection, or amputation. The radiosensitivity of the tumor is low.

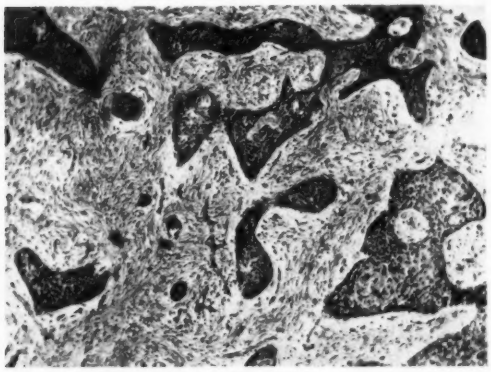

Fig. 3. Photomicrograph, low power, showing tissue removed at the first operation in 1929. Cords of epithelial cells, with central cystic spaces in a loose stroma of fibrous tissue, are seen. ×70.

Roentgenologically, the tumor appears as a polycystic, expanding central tumor with sharp outlines and a fine trabecular pattern. No periosteal reaction or new bone formation is seen. There are no worn or eroded margins. A fine honeycombed appearance is often seen which is not usually present in bone cysts or giant cell tumors. The differential diagnosis is difficult, and the rarity of the tumor makes it even more so. No

Fig. 4. Roentgenograms, April 10, 1934, show an extensive recurrence of the tumor, with complete replacement of the bone graft.

case, to our knowledge, has been diagnosed before the pathological examination was made. Even then, many competent, well trained pathologists have encountered difficulties in making the correct diagnosis.

We believe that the following case fulfills the diagnostic criteria of an adamantinoma.

D. D. (Bone sarcoma registry No. 1819), a white male, 45 years of age, was seen by the late Dr. Hunkin in 1929 because of a complaint of weakness of the right arm of several months' duration, and fleeting, burning pains which radiated up and down the entire arm. The patient had fractured his right arm just above the wrist on two occasions, once in 1902 and again in 1905. The injury in 1905 resulted from a blow received in a football game. The roentgenograms were subsequently destroyed. Several months after the second injury, the patient noted deformity of the right elbow and slight limitation of motion, neither of which had caused any real disability. Aside from

Fig. 5. Roentgenograms, September 24, 1934, show further extension of the tumor with destruction of the cortex of the ulna.

these injuries, the past history was noncontributory. General physical examination in 1929 was essentially negative. The right arm presented a palpable dislocation of the head of the radius with limitation of supination and a diffuse swelling over the ulnar side of the forearm. Roentgenographic examination showed marked lateral bowing of both the radius and ulna with a dislocation of the head of the radius which appeared to be of long standing (Fig. 1). The proximal end of the ulna was widened and articulated fully with both humeral condyles. The shaft of the ulna was diffusely expanded throughout by a honeycombed rarefying process which extended to within an inch of either end of the ulna. In the distal 3 inches of the expansion the cortex was extremely thin, with large round and smaller foam-like lobulations. The remainder of the involved area had a more dense appearance with definite honeycombed trabeculation. No periosteal reaction was evident.

A resection of the lower portion of the shaft of the ulna with the implantation of an 8 inch tibial graft was performed on September 24, 1929 (Fig. 2). The patient made an uneventful recovery and had good use of his arm but with slight limitation of supination. During the next 4 years, he was without pain, discomfort, or other complaint referable to the right arm.

*Pathological report, October 4, 1929.* The specimen consisted of a mass of tissue removed from the ulna measuring approximately 4½ by 2 by 1 centimeter. On section, the

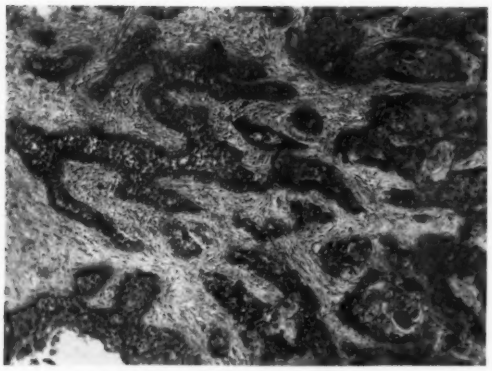

Fig. 6. Photomicrograph of a section of the specimen removed on November 26, 1934. The area is similar to the tumor removed in 1929. Changes suggestive of squamous cell carcinoma are seen in the lower right hand corner. ×70.

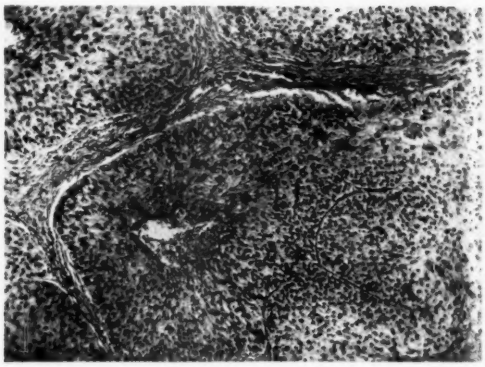

Fig. 7. Photomicrograph of the tumor removed on November 26, 1934. This shows a cellular area with scanty stroma. Peripheral columnar cells and a central stellate zone with cystic spaces are evident. Many mitotic figures are present. ×70.

bulk of the tissue presented a uniform grayish white, finely granular substance. At one end of the specimen some fine points of calcification were encountered. This presumably was where the bone had been invaded. Sections were taken from all points.

The sections showed an unusual type of tumor. The stroma was composed of a pale staining, primitive appearing fibrillar connective tissue—not unlike the mesenchyme seen in the umbilical cord. Somewhat irregular, elongated spindle shaped nuclei, some dark and slender, and others plumper with a delicately staining stippled chromatin, lay in a very delicate eosinophilic fibrillary stroma.

Through this coursed a variety of tubes and cords of endothelial cells forming imperfect vascular spaces with single or multiple layers of cells that showed elongated dark nuclei, and a more condensed eosinophilic cytoplasm. Some contained what were thought to be red cells. Cords of similar cells were seen without any visible lumen, and all gradations existed between the two types. Some of the cells were of distinctly polyhedral outline and of pavement type. Swelling and hyaline degeneration of some of the cells gave an appearance simulating epithelial pearl formation. As a matter of fact, cells of the stroma and those forming the cords and vascular spaces seemed to be of the same origin and intermediate forms were prevalent. The method of growth seemed to be the factor determining the exact morphology. Tangential sections of these endothelial cords resembled giant cells.

Cells resembling plasma cells and lymphocytes were present singly and in small groups lying both within and outside endothelial channels. Some of these presented a hemoglobin tint to the cytoplasm and were believed to represent differentiation of the primitive cells into nucleated red cells and polyblasts. Mitoses were fairly frequent in the endothelial cells. Bits of bone were present in some sections but the tumor did not show evidence of bone formation (Fig. 3).

The diagnosis was "mesenchymal endotheliomal."

During March, 1934, the patient noted a recurrence of all the complaints previously mentioned and roentgenograms were again taken which showed extension of the rarefying process in the ulna and complete replacement of the bone graft by the same condition (Fig. 4). One month later he developed a tender, firm, nodular swelling over the middle of the old operative scar. Roentgen therapy resulted in disappearance of the pain and swelling, but these recurred after a short interval and failed to respond to further roentgen treatment. The patient entered the University of California Hospital in October, 1934, for complete study. No further relevant history could be obtained. General physical examination revealed no abnormalities except for the right arm. An operative scar, 10 inches in length, was present over the ulna. A lump, about 2 by 2 by 1 centimeter in size, was present in the middle of the scar; it was not attached to the skin, but was firmly fixed to the underlying bone. The lump was tender to palpation but no inflammatory signs were present. The entire arm was diffusely atrophied and supination was limited. Complete blood count was within normal limits. Wassermann and Kahn tests were negative. Roentgenograms of the chest were negative. Aub studies showed a

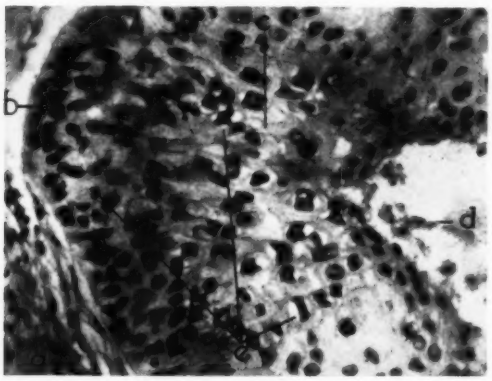


Fig. 8. Photomicrograph, high power, of a portion of the same section as shown in Figure 7. *a*, Stroma; *b*, peripheral columnar cells; *c*, central transitional cells with "stellate" anastomosing processes; *d*, cystic space with cellular débris; e, mitotic figures. ×310.

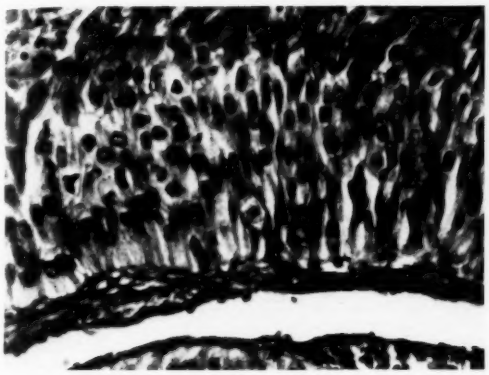

Fig. 9. Photomicrograph, high power, of the recurrent tumor (1934) showing the detail of the high columnar cell layer resembling enamel epithelium. ×310.

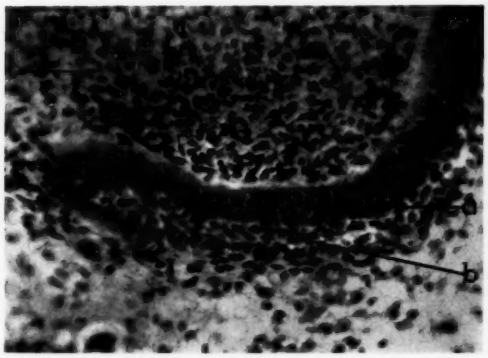


Fig. 10. Photomicrograph, high power (×450) of a part of the dental lamina of a 1 day old rat, showing the type of structure reproduced by adamantinoma. a, Enamel epithelium; b, "stellate" area; c, primitive mesenchymal tissue.

normal balance of calcium and phosphorus metabolism. Blood serum calcium was 10.92 milligrams per 100 cubic centimeters; phosphorus, 3.54 milligrams, and phosphatase, 8.35 milligrams.

The patient refused further surgery at this time and was discharged from the hospital. During the following month the pain increased greatly in severity and the entire arm became tender. Roentgen examination showed complete absence of bony cortex over the tumor with extension into the soft tissues (Fig. 5). The patient submitted to surgery, and at another hospital, an attempt was made to resect the ulna and the contained tumor. This could not be cleanly done, and some of the tumor was allowed to remain, the tumor having extended into the muscles and subcutaneous tissues.

*Pathological report, November 27, 1934.* The specimen consisted of a fusiform tumor 11 centimeters long and 5 to 6 centimeters in diameter at its greatest thickness, to the end of which were adherent short segments of bone. The mass was rather firm, rubbery, and had no definite limitations. It appeared to have arisen in the medullary portion of the bone, to have destroyed the cortex for a distance of 11.5 centimeters, and to be extending along the medula invading and destroying the shaft. On section it was a whitish gray, somewhat fibrous tissue. The central portion presented small light yellow, circular areas of degeneration. Small fragments of muscle and tendon were adherent to the tumor and were inseparable therefrom, suggesting the invasion of soft and tendinous tissues. Both segments of the ulna were partially fragmented at the junction with the tumor. The raggedness of the surface of the tumor suggested incomplete removal. At the lower end of the tumor there was a circular silver wire partially embedded in the tumor tissue. Sections from various portions of the tumor mass showed a very cellular structure. Many strands and clumps of elongated and spindle shaped cells were arranged in a somewhat epithelial pattern upon a moderate amount of fibrous stroma. The tumor cells had a clear staining cytoplasm, an elongated or ovoid, finely granular nucleus with a small nucleolus. In areas the masses of tumor cells showed small areas of central degeneration. In other areas small circular whorls were formed. At the borders and central portions of some tumor masses the cells were somewhat enlarged but resembled the majority of other cells in pattern.

The diagnosis was "endothelial bone tumor, probably angiosarcoma" (Figs. 6, 7, 8, 9).

The wound healed readily, but pain and tenderness returned 2 months later. Amputation was performed through the lower humerus. The patient has been seen at regular intervals since the amputation was performed, and has remained in perfect health with no evidence of recurrence or metastasis for the past 6 years. Unfortunately, the specimen obtained at the time of amputation was destroyed

This case was submitted to the committee on bone sarcoma of the American College of Surgeons. The opinions submitted ranged from "angioendothelioma" to "typical squamous cell carcinoma." Most of the committee favored metastatic carcinoma. No agreement was reached, however, and the case was listed under the original diagnosis of angiosarcoma.

Upon reviewing the microscopic sections and the patient's case history, we were struck by the long period of survival in spite of the obvious pathological malignancy of the tumor. The first sections (1929) seemed to us to be typical of adamantine epithelioma. The second group of slides (1934) present a very different pattern but contain cells which could be derived only from epithelium and other zones of definite ameloblasts, degenerating stellate cells and many cyst-like spaces.

The sections were re-examined by the pathologists, Drs. Rinehart and Bartlett, who now agree that the neoplasm is an adamantinoma.[1] In view of the fact that a careful search of the literature produced no other case of such a tumor arising in the ulna, it is not surprising that the diagnosis

[1]James Rinehart, Edwin I. Bartlett, and Charles L. Connor (deceased) were of invaluable assistance in the pathological examinations. Dr. Judson Sale kindly granted his permission to report this case.

was not made at first even by such well trained and experienced pathologists.

The apparent invasive malignancy of the recurrent tumor is corroborated by the microscopic findings. The marked cellularity, the large cells with hyperchromatic nuclei and the mitotic figures are malignant characteristics. These are all more prevalent in the recurrent than in the original tumor. Although this degree of degenerative change is not often seen in adamantinoma, it is easy to conceive that such a metaplasia might occur in any epithelial tumor. The pathological findings, the long duration of symptoms, the recurrence of the tumor after 5 years, the absence of any other neoplastic process, and the failure of the tumor to metastasize indicate to us that adamantinoma is the correct diagnosis.

SUMMARY

1. Adamantinoma of the long bones is a rare entity.

2. The pathological, clinical, and roentgenographic characteristics of the tumor are described.

3. A case of a primary adamantinoma of the ulna is reported. We believe this to be the first recorded case of this tumor arising in a long bone other than the tibia.

REFERENCES

1. Baker, A. H., and Hawkley, L. M. Brit. J. Surg., 1930–1931, 18: 415.
2. Bishop, E. L. South. M. J., 1937, 30: 571.
3. Casini, A. Policlinico (Sex. Chir.), 1935, 42: 338.
4. Fischer, B. Frankf. Zschr. Path., 1913, 12: 422.
5. Geschickter, C. F., and Copeland, M. M. Tumors of Bone. New York: The American Journal of Cancer, 1936.
6. Holden, E. Jr., and Gray, J. W. J. Bone Surg., 1934, 16: 401.
7. Rankin, John O. J. Bone Surg., 1939, 21: 425.
8. Rehbock, D. J., and Barber, C. G. J. Bone Surg., 1938, 20: 187.
9. Richter, C. S. Zschr. Krebsforsch., 1930, 32: 273.
10. Ryrie, B. J. . Brit. M. J., 1932, 11: 1000.
11. Thomas, R. G. Brit. J. Surg., 1939, 26: 547.
12. Wolfort, Benjamin, and Sloane, David. J. Bone Surg., 1938, 20: 1011.

# TRAUMATIC AND SPONTANEOUS FRACTURES IN EXOPHTHALMIC GOITER

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INSTANCES of spontaneous fracture in cases of exophthalmic goiter are extremely rare. To date, only 7 cases have been reported which in itself constitutes adequate evidence of either its great rarity or, at least, its infrequent recognition. In the majority of instances in which it has occurred, the hyperthyroidism has been marked, long continued, and accompanied by extreme demineralization and decalcification of the bony skeleton.

So far as we can determine, the case here reported constitutes the only one in which both traumatic and spontaneous fractures have occurred following earlier partial removal of the thyroid gland. Twelve years following operation the first fracture occurred. It was traumatic in origin. The two others appeared in rather quick succession, were simultaneous as to time, and spontaneous in origin. On roentgen examination, all the bones of the body were found to be decalcified to a very remarkable extent.

In 1891 von Recklinghausen first described the demineralization of the skeleton in a case of hyperthyroidism of many years' duration. Subsequently, Koeppen and Askanazy reported similar cases. In these early cases, the pronounced demineralization was apparent at autopsy when they were studying the bones. It was some years before this picture of general osteoporosis was demonstrated clinically by the roentgenologists (4, 12). They pointed out the marked decrease in the density of the bones with the thinning of the cortex.

In 1928 Plummer and in 1929 Dunlap and Moore reported 5 cases of hyperthyroidism in which there was pronounced demineralization of the skeleton. In 2 cases, the bone changes were so extensive, that metastatic malignancy was considered. Many other contributors (8, 9, 10, 17) have reported cases of demineralization in this disease. It is generally believed that the demineralization involves practically the entire skeleton. However, the small and flat bones usually show the change first, and later it is evident in the spine and long bones. Shrinking of the general stature (5), kyphosis and flaring of the lower ribs (13) have all been reported.

Aub and his co-workers reported an increase in the excretion of calcium and phosphates in clinical hyperthyroidism. They found the average excretion in cases of thyrotoxicosis 231 times greater than that in a normal individual. The serum phosphatase has been found to be elevated in cases of hyperthyroidism. Aub did not believe that the excessive excretion of calcium could be attributed entirely to the elevation of the metabolism as it does not occur in patients with other diseases accompanied by an increased metabolic rate. It was also noted by Aub that the excretion returned to normal after the thyrotoxicosis had been controlled. They concluded that the most likely cause for the demineralization is a direct stimulating effect of the thyroid gland on the calcium deposits in the bones. Others (14) believe that the demineralization is secondary to a disturbance in metabolism of the carbohydrates. It is generally agreed that this condition is found only in cases of long standing hyperthyroidism. Pain, which occurs in the involved parts, is the outstanding symptom associated with these skeletal changes.

Bartels and Haggart reviewed the literature and found 5 cases of long standing hyperthyroidism in which spontaneous fractures had occurred, and they added two of their own. In several instances, the fractures occurred in the humerus (7) and other long bones. In both cases of Bartels and Haggart, the fractures occurred in the vertebrae. In their first case there was a crush of the first lumbar vertebra, and in their second case the crush was located in the 6th and 10th dorsal vertebrae. The pain, associated with these lesions, is relieved following thyroidectomy, but the recalcification of the skeleton is a very slow process. In 1 case (13) previously reported, the osteoporosis was progressive even after thyroidectomy. Bartels and Haggart made roentgenograms a year after thyroidectomy and there was no recognizable bone recalcification. We should bear in mind, that these patients had had a negative calcium balance for many years

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Aided by grant from the Daland Fund, American Philosophical Society.

Fig. 1. Roentgenograms illustrating, a, demineralization of the femur, tibia, and fibula; b, the small bones of the hand and the ulna and radius.

and that with a small daily intake of calcium, it would take considerable time for sufficient redeposition of calcium to have occurred to show by the x-ray.

In addition to thyroidectomy, the fracture itself is treated as indicated by the lesion encountered. Calcium is administered in great quantities daily in an effort to overcome the deficiency which we have found in the osseous structures. As pointed out by Bartels and Haggart, a well balanced diet is important at all times.

### CASE REPORT

H. J., male, aged 36 years, was referred by Dr. M. S. of London, Canada, to one of us (L. G. R.) in June, 1940. The chief complaint was intermittent pain and stiffness in the back, in the region of the first lumbar vertebra. The patient also complained of nervousness, sweating and bulging of the eyes. The family history revealed nothing of significance. The patient had had the ordinary diseases of childhood, i.e., measles, mumps, whooping cough, and chicken pox. His tonsils had been removed many years ago and the septum had been straightened. He also had had an appendectomy. Patient had suffered from a "bursa in the neck" which was opened when he was 14 years of age. Thyroidectomy for exophthalmic goiter had been performed elsewhere in 1926.

The patient is married, has two children, aged 5½ years and 6 months. He is happy in his work, drinks very moderately, uses tobacco, but not to excess. He has taken Lugol's solution intermittently over a number of years. Venereal infection is denied.

In the spring of 1926 (March 6) this patient had a severe attack of "flu" with high temperature. He became nervous and lost 15 pounds in weight though his appetite was good. His eyes became more prominent. The patient stated that he withstood cold exceptionally well and wore fewer clothes than most people. He complained somewhat of thirst and said that his pulse varied from 120 to 130 a minute. His blood pressure was 135/90. The heart was normal except for sinus arrhythmia, extra systoles and tachycardia; urine was normal; basal metabolism was plus 32. A marked tremor was present in the extended fingers. In November, 1926, a diagnosis of exophthalmic goiter was made.

On December 2, 1926, this patient was subjected to a partial thyroidectomy elsewhere. Several months after operation the basal metabolism was minus 30. He was given thyroid extract over a period of 3 months, at which time the basal metabolism had returned to normal. At the end of the first postoperative year the metabolic readings were plus 38 and plus 35.

In September, 1928, he again consulted his physician. The exophthalmos had become more marked, his pulse was in the neighborhood of 100, his weight was unchanged, and the blood pressure was 120/70. The electrocardiogram was normal but the voltage was slightly low; metabolism rate was plus 23. The opinion was expressed that there had been a recurrence of the hyperthyroidism, and a return to the surgeon for further treatment was advised.

The patient continued through the intervening years without much change in his clinical condition. He suffered intermittently from frequent mild attacks of diarrhea. His bowels were almost invariably loose and the stools unformed. The patient had an aversion to milk and cheese, and the calcium intake was, therefore, extremely low.

On January 13, 1940, the patient slipped on ice and fell only a short distance but he suffered immediately from excruciating pain in the back. On admission to the hospital x-ray examination revealed the presence of a fracture of the first lumbar vertebra, plus generalized decalcification of his bones. Several days after his admission to the hospital his pulse increased to 150–160 per minute. The patient became exceedingly nervous. The condition looked like a typical hyperthyroid crisis. Because of his decalcification and general bodily conformation, he was treated by hyperextension on a fracture board without the use of a cast. About March 7 he developed an acute sinusitis while in bed, which again increased his pulse rate to 150. He was confined to the hospital from January 13, 1940, to March 27, 1940. His activities were greatly restricted. He was furnished a Taylor brace which he used for the next 6 weeks.

Laboratory examinations revealed the blood and urine to be essentially normal. Blood calcium and serum phosphates were within normal limits. Determination of the basal metabolic rate was attempted but proved unsuccessful because of the inability of the patient to breathe into the bag.

During his hospitalization he received calcium phosphate and small doses of Lugol's solution.

About June 1, 1940, following a "snooze on a train" he awakened with considerable stiffness and pain in the back, for the first time since resumption of partial activity. Roentgenological examination showed marked changes, with collapse of the 5th and 9th thoracic vertebrae. These lesions were not present on the former x-ray film.

On the patient's arrival in Philadelphia, he was admitted to the Presbyterian Hospital. His height was 5 feet 10 inches and his weight 185 pounds. His eyes were very prominent. Von Graefe's sign was positive; pulse rate was 144, blood pressure 130/60. The thyroid could not be palpated.

The lungs were normal on superficial inspection, palpation, percussion and auscultation. The heart was normal in size, shape, and position, and there was no disturbance in rhythm.

The chest and abdomen were both prominent. A scar was noted over the appendiceal area; no masses were felt or seen in the abdomen. The patient was rather hairy, with a heavy beard. The skin was bathed in sweat; tremor of the hands was marked and the knee jerks were active. The gonads were normal.

At this time the basal metabolic rate was plus 43. Blood cholesterol was 107. Blood count showed red blood cells, 4,070,000; hemoglobin was 16.24 grains or 104 per cent; white blood cells, 3,800; polymorphonuclears, 59; lymphocytes, 35; monocytes, 4; and eosinophiles, 2. The urinalysis was negative except for a trace of albumin. The urine was negative for Bence-Jones protein. The urinary calcium for 24 hours was 321 milligrams, hydrogen ion concentration of blood 7.4. Blood chemistry analysis showed calcium, 10.5; phosphorus, 2.1; phosphatase, 6.25. Second examination showed calcium, 10; phosphorus, 2.1; phosphatase, 5.95; protein of the blood, 7; albumin 5.8; globulin, 1.2. The stools were semiliquid, large in amount with no abnormal constituents. Capillary permeability and bleeding time were normal.

Comprehensive roentgen studies of the osseous system showed generalized demineralization which was considered most likely to be due to hyperthyroidism. Paget's disease and malignancy appeared to be excluded; multiple myeloma was practically excluded.

A small nodule was encountered on the left side of the neck on June 29, 1940. It was explored by one of us (F. A. B.) and was found not to be a parathyroid gland.

The clinical diagnosis in this case was hyperthyroidism with marked decalcification, the patient exhibiting both traumatic and spontaneous fractures. Hyperparathyroidism, multiple myeloma and malignancy were considered, but were considered to be unlikely. It was thought perhaps that decalcification was the result of three factors: (1) prolonged continuous hyperthyroidism, (2) continuous but mild diarrhea, (3) aversion to foods rich in calcium resulting in meager calcium intake.

The roentgenograms suggested the possibility of multiple myelomas. To rule this out the patient was sent home, advised to remain at rest, take a diet rich in calcium and phosphorus. Calcium gluconate was administered parenterally and by mouth. Cod liver oil and viosterol were also employed. After 2 months on this regimen no evidence of improvement was apparent; the patient returned to Philadelphia, laboratory studies were repeated with results that were practically identical. The basal metabolic rate was plus 39. Surgery was advised and after adequate preoperative preparation an exploratory operation was performed by one of us (F. A. B.) on September 11, 1940. After the ribbon muscles were retracted, a mass could be palpated in back of the trachea on the right, which upon exploration proved to be a large adenomatous right lobe. This was removed. A small pyramidal lobe was located high in the neck and was excised. On the left, another portion of adenomatous thyroid was removed substernally and behind the trachea.

The specimen consisted of three pieces of thyroid tissue, 5 by 3, 5 by 3 and 2 by 2 by 1 centimeter, respectively, and weighing 50 grams. The lobes were well encapsulated, and they consisted of moist, glistening, brownish-yellow, granular lobulated tissue in which were hard, white, calcified nodules, small cystic spaces, and soft yellowish pink nodules.

Microscopic examination of the thyroid tissue revealed marked variation in shape and size of acini. The lining cells are of the low cuboidal and occasionally low columnar type, rarely being thrown up into a spur. The colloid has not completely been restored and much of it assumes a granular appearance. There are focal accumulations of lymphocytes and in the interspaces, not showing, follicle formation. Several of the sections show a well encapsulated mass bordered by compressed and atrophic thyroid tissue. Portions of this mass display fairly typical thyroid tissue which presents the changes described before. Other portions have a collagenous stroma supporting tiny acini lined by small hyperchromatic cells resembling the fetal type. There is no evidence of malignant change within the adenoma.

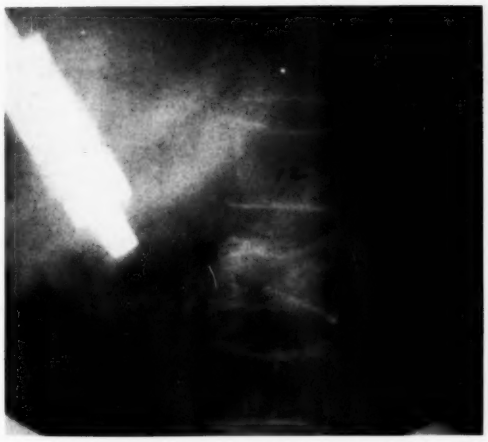

Fig. 2. Roentgenogram of the spine illustrating demineralization and traumatic fracture of the first lumbar vertebra.

The diagnosis was toxic nodular goiter with incomplete involution.

Following operation the patient made an uninterrupted recovery. At the end of 2 weeks the symptoms of hyperthyroidism had almost completely disappeared. The basal metabolic rate had decreased to plus 13, the pain in the back had diminished considerably, and the patient walked about the room with relative comfort. Shortly after, the patient returned home; for the first time in many months he was able to go to the table for meals, go up and down stairs and get out for short walks, without any discomfort or distress.

Six months following operation, his basal metabolic rate had fallen to a minus 8. He was placed on 1 grain of desiccated thyroid for a few weeks. Ten months after operation, the follow-up visit showed the patient had been completely relieved of the symptoms of thyrotoxicosis. His activity had returned to a normal routine. The brace was discarded 7 months after operation, and all symptoms which were relative to his back had disappeared. The exophthalmos had diminished and he had gained 17 pounds in weight.

There have been many x-ray studies subsequent to operation, which revealed that the fractures in the vertebra had united and there was a very slight increase in the calcium in the vertebral bodies. The generalized demineralization was still present with very slight apparent improvement in calcium content.

Fourteen months after operation the symptomatic cure was complete. The patient, formerly a helpless invalid, had been restored to perfect health and was back at work on a full time basis. The recalcification of the bones, however, in this individual, as in other cases reported in the literature, was tardy and unimpressive, as revealed by the x-ray. More time is needed before a final statement relative to remineralization can be made.

X-ray examination of the spine in April, 1942, revealed a moderately improved mineral content of the bone structure since December, 1940.

## REFERENCES


1. Askanazy, M. Quoted by Hunter. Loc. cit.
2. Aub, J. C., Bauer, W., Heath, C., and Ropes, M. J. Clin. Invest., 1939, 7: 97–137.
3. Bartels, E. C., and Haggart, G. E. N. England J. M., 1938, 219: 373–378.
4. Bernhardt, H. Münch. med. Wschr., 1927, 75: 432.
5. Coryn, G. Arch. internat. méd. exp., Par., 1936, 11: 135, 291.
6. Dunlap, H. F., and Moore, A. B. Med. Clin. N. America, 1929, 12: 1511–1519.
7. Gottlieb, F., and Schachter, M. Presse méd., 1937, 45: 277–278.
8. Gurshman. Quoted by Gottlieb and Schachter.
9. Henricke. Quoted by Gottlieb and Schachter.
10. Hunter, D. Lancet, Lond., 1930, 1: 947–957.
11. Koeppen, H. Neur. Zbl., 1892, 11: 219–220.
12. Kummer, R. H. Zev. méd. Suisse rom., 1917, 37 439–463.
13. Means, J. H., Hertz, S., and Lerman, J. Ann. Int M., 1937, 11: 429–436.
14. Moehlig, R. C., and Adler, S. Surg. Gyn. Obst 1937, 64: 747–757.
15. Plummer, W. A. Proc. Mayo Clin., 1928, 3: 119–121
16. von Recklinghausen, F. Die fibrose oder defor mirende Ostitis, die Osteomalacie und die oste plastische Carcinose, in ihren gegenseitigen Bezie hungen. Festschr. F. Rudolf Virchow. Pp. 1–80 Berlin: George Reimer, 1891.
17. Snapper, I. Surgery of the parathyroids. Congr fr. chir. 42 Session, Paris, 1933.

# INTERNAL WIRE FIXATION OF JAW FRACTURES

## Second Report, with Note on External Bar Fixation

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SINCE the preliminary report,[1] this method has continued to be of major service in the fixation of difficult jaw fractures. The necessity for wide open reductions has almost been eliminated, and complicated dental appliances are avoided.

The patients appreciate being able to open and close their mouths throughout the healing period (Fig. 1), and the added cleanliness is an advantage in the care of any lacerations inside. It has been easier to maintain the airway in patients with much upper neck swelling from hemorrhage or infection, and tracheotomy has been avoided in one instance. Its use might be desirable in military personnel who are apt to be seasick, and in patients who require a general anesthetic for other injuries. However, patients with associated condyle fractures should have additional interdental fixation to the upper jaw or some method of holding the chin forward in proper occlusion. This seems to be the simplest and best treatment for this fracture, although many recommendations have been made, from immediate open operation to doing nothing.

*Sequelae and complications* have been minimal and there has been no extensive osteomyelitis. There have been occasional late small abscesses beneath the fracture sites, as may occur with any other method of treatment. A few instances of small localized areas of osteomyelitis occurred on the undersurface of symphysis fractures, with the late extrusion of a few small bone chips. It is possible that these resulted from the cross-fracturing of the inferior cortex, either when the wire was drilled in or later from chewing, as they have all occurred in instances in which the wire was put in so low that only the cortex was left below it. This complication has not developed in symphysis fractures in which the wire was drilled through higher in the bone, and as the nerve supply to the teeth is relatively high in front of the mental foramina, it is suggested that a sufficiently strong bridge of bone should be left beneath the wire in this location.

The skin holes have healed without noticeable marks in almost all instances, though it may be best to push the fat pad of the chin up out of the way when wires are put directly through this

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[1]Internal wire fixation for fractures of the jaw; preliminary report. Surg. Gyn. Obst., 1942, 74: 227.

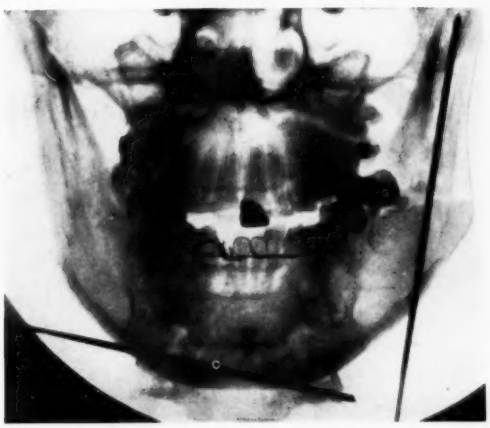


Fig. 1. Fixation of double fracture with two internal wires and an anterior dental arch. Angle fracture was so far back that the wire was drilled vertically through it up into the ramus. Patient could take soft foods from the first.

Fig. 2. Displaced symphysis fracture and depressed orbital floor. Open mouth treatment of lower jaw with internal wire and anterior wire arch. The orbital floor was elevated through the antrum and held with an iodoform pack. The healed skin holes are scarcely visible, upper right illustration.

region (Fig. 2). No instances of nonunion have occurred, even though several of the patients were first seen late after infection had developed. This brings up the interesting possibility that the drilling across the fracture site may aid osteogenesis.

*Vitallium and other alloys* have been considered, but the stainless steel wires have continued to be satisfactory. They should be of the same material throughout and polished, rather than coated. The smallest size that will produce the necessary rigidity in each instance should be used. Wires of .035 inch or .045 inch diameter are generally used, though ones up to .08 inch have been employed. A three-sided point seems easier to start in the bone than the usual spade point, and the sides of the point should have a long bevel. This was recommended by Dr. C. H. Crego.

*Reaction around the wires* has been so slight that many patients have neglected to keep even a small dressing over the ends, though this is advised. Even after 6 weeks, they often have to be rotated many times and considerable traction used for their extraction. Threaded wires have to be unscrewed throughout their length for removal, and most of the removed wires have shown no evidence of corrosion. Because of the persistent tightness of the plain wires, the threaded ones are seldom used, though they probably give a slightly more rigid fixation.

## OPERATION

*The best possible asepsis* should be maintained during the insertion of the wire. One person usually holds the fragments in place with his hands while another one drills the wire through. When teeth are present, it may be easier for the one holding if a dental arch is put on first. This is a simple anterior wire arch of No. 26 stainless steel wire. One wire is looped around a back tooth on each side and the ends twisted together for 2 to 3 inches. The two wires are then anchored together in front with a few turns, and the arch is held firmly with finer wires, No. 28, around it and a few other teeth. This arch gives a second plane of fixation and helps hold any block detachments of the teeth and alveolus. It has to be omitted, of course, when there are not sufficient teeth.

The drill operator should be careful not to contaminate his gloves or the wire with mouth secre-

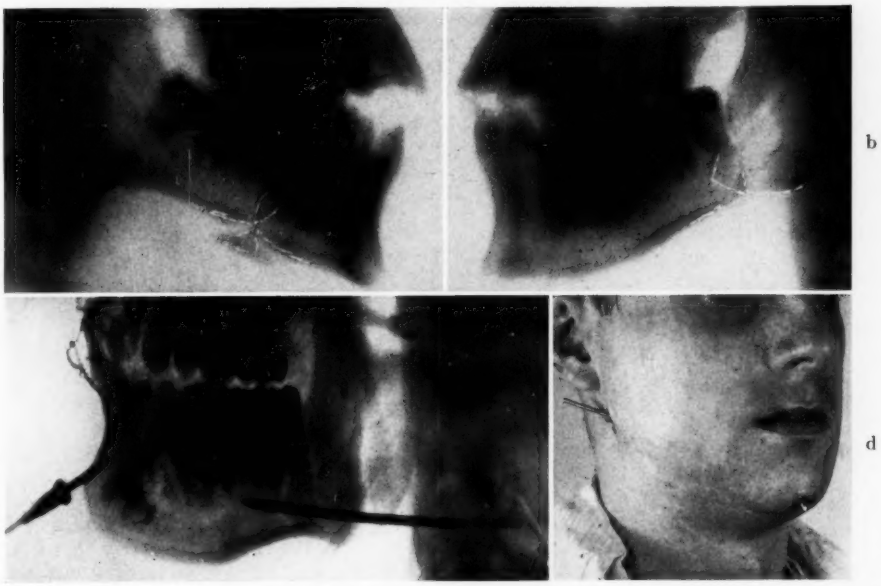



Fig. 3. a, b, Displaced fractures at mental foramen and opposite angle with main fragment hanging down. c, d, Fixation with 2 internal wires and an arch bar. Patient able to open and close mouth throughout treatment.

tions and the skin should be prepared again just before the point is inserted. An ordinary motor-driven bone saw, with a chuck to accommodate the wire, is most often used. Dental engines do not seem to have enough power. If the fragments can be held in a sufficiently stable manner, an ordinary carpenter's hand drill can be used at times. The rotary speed of the wire should be enough for easy penetration but not so fast as to possibly produce heat necrosis of the bone. In this connection, it is thought that a too slow forward speed or a dull point may produce an excessive amount of heat in one area. Threaded wires must be put in at a low speed as they definitely catch and take hold in the cortex and go in so fast as to be out of control at a high speed.

A nick is made in the skin and a small area of periosteum is denuded where the wire is to be started. The most difficult place to get started seems to be on the back of the ramus when drilling forward through an angle fracture. To do this, the head is usually rotated to the opposite side and the lobe of the ear held up out of the way. The wire is cut down to the minimal necessary length

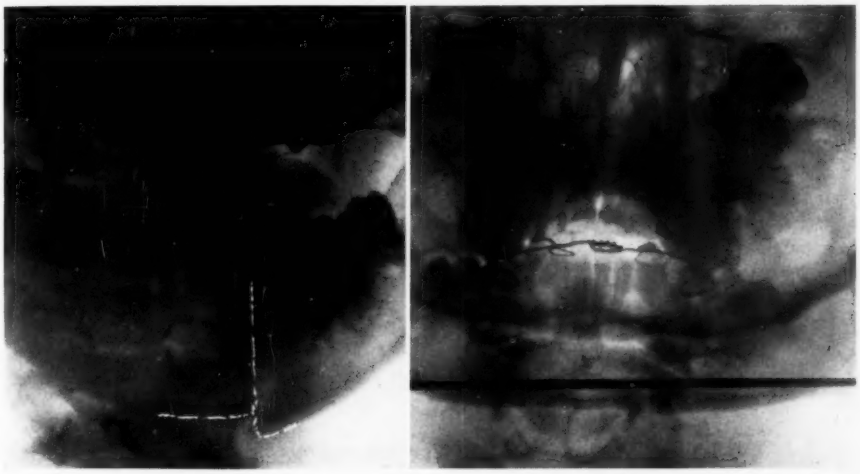
Fig. 4. Fractures in front of both angles in a man with very few teeth. Long posterior fragment on right side edentulous and one on left side contains just one tooth. Interdental wires also were left on a few days. Patient returned to work within a period of 10 days. Solid union obtained.

Fig. 5. a, Bilateral fracture in a totally edentulous jaw. Patient was able to put in upper and lower dental plates and eat soft foods after the first week, though the lower plate was painful if left in continuously. Returned to work in 2½ weeks. b, Angle and mental foramen fractures in an almost edentulous jaw. Open reduction avoided. c and d, Fixation of an almost edentulous jaw in an insane man, which was solid enough to hold without any co-operation.

to prevent any lateral "whip" when it is rotating, and the point is inserted against bare bone. The drill operator may then hold the wire near the tip with a small piece of greased gauze or any other type of "bearing" to steady it. The wire may be drilled on through the cortex and skin in front, or if a good length of jaw is engaged, the point may be just left in the bone (Fig. 3). In angle fractures which are so far back that they tend to be in the ramus, it may be better to start the wire on the lower border of the jaw and drill vertically upward into the ramus, staying outside of the third molar (Fig. 1). In the case of long posterior fragments, it may be less difficult to start the wire just in front and below the mental foramen and then to drill backward through the fracture (Fig. 4).

The work is most often done under novocain deep-block anesthesia with or without a supplementary basal anesthetic. Even with the lower jaw completely anesthetized, a patient with teeth can usually tell when his normal occlusion is restored, and this may be of help at times.

*Ordinary interdental wiring is still recommended* for fixation of simple fractures when enough teeth are present. The internal fixation is used when there are insufficient teeth, or for more severe fractures to avoid complicated appliances and wide open reductions, or when it is desirable to leave the mouth open. It is probably the simplest method for fixation of displaced edentulous jaws or fragments (Fig. 5), including the posterior fragments of angle fractures. A further use is as a second plane of fixation (in addition to an arch bar



a b

c

Fig. 6. Severe injury with basal skull fracture, broken condyle and symphysis, and depressed fractures of both orbital floors. Treatment delayed 1 week until patient was rational and not vomiting. a and b, Fixation used, interdental wires being added because of condyle fracture. Both orbital floors elevated through antrum and held with iodoform packs beneath them. c, After removal of packs and interdental wires.

on the teeth) in symphysis fractures to prevent "rocker" motion (Fig. 6). It has also been used for certain upper jaw fractures (Fig. 7) and (with larger pins) as a means of holding the mouth open for skin grafting inside (Fig. 8).

In fractures seen late with large abscesses present, the latter have been drained and the fixation has been done a few days later, an effort being made to avoid going through infected soft tissues in so far as possible.

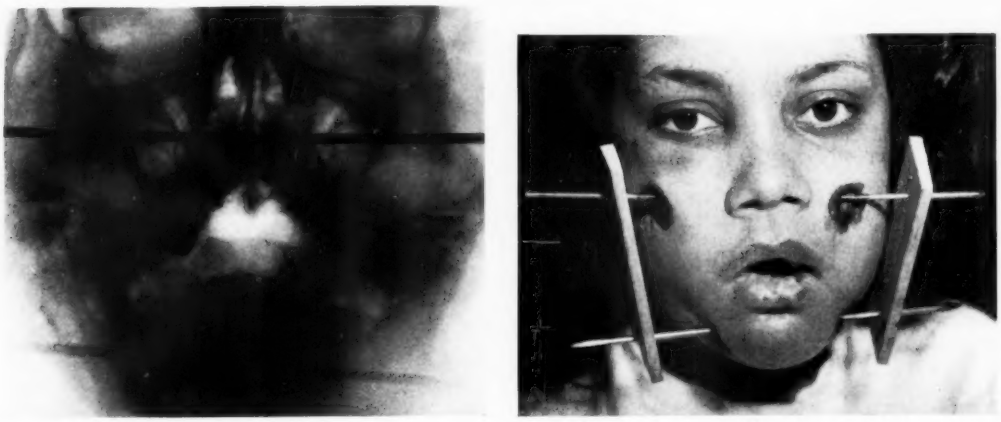
### EXTERNAL BAR FIXATION

*Severe, shattering injuries* may still tax the ingenuity of the operator if the loss of fragments and continuity and the necessity for late bone grafting are to be avoided. They may require combinations of interdental wiring, arch bars, internal wire fixation, and external bars applied with wood screws.

The latter method consists of putting a wood screw through the outside into each of the larger

a b

Fig. 7. Severe facial injury with partial obstruction of airway from swelling in upper neck, necessitating operation in semisitting position. The entire left upper jaw was hanging down in the mouth, being separated in the midline of the palate and transversely through the middle of the antrum. Symphysis widely separated and submental region full of blood. a, Method used for fixation of bones. Soft tissues of palate were sutured. b, Patient was in hospital 8 days, began to eat soft foods in few days and returned to work in 3 weeks. Tracheotomy possibly avoided.



a b

Fig. 8. Old lye burn with inside of mouth almost entirely filled with dense scar. Floor of mouth and tongue grown solidly to palate so no opening of jaws was possible. Mass of scar excised from mouth to permit opening, then held open to permit later skin grafting by means of two small ($\frac{3}{32}$ inch) Steinmann pins and wooden blocks.

bone fragments, and then attaching all of the screws to a rigid external curved metal bar (Fig. 10). They can be attached to the bar by means of separate lugs, or by means of a compressible slot which can be soldered to each of the screws beforehand. A small nick is made in the skin and a drill

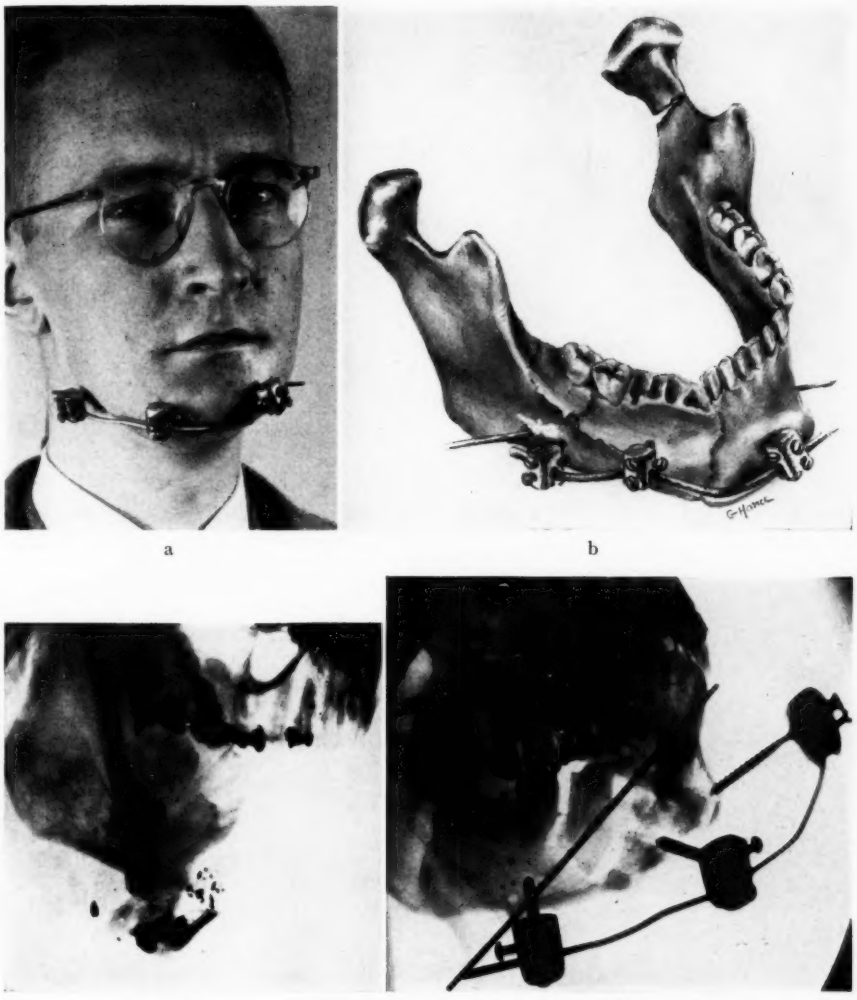


Fig. 9. Shattering jaw injury with partial collapse of airway. Arrived sitting in an ambulance with accompanying physician holding jaw forward when necessary. Large fragment displaced down into soft tissues of the neck. All major fragments saved, reduced, and immobilized with external bar and internal wire. A few interdental wires were also placed where teeth were present, because of condyle fracture. Solid union with good occlusion obtained. Late bone grafting avoided. Lugs designed by Dr. James A. Brown.

hole into the cortex to aid in starting the screws, but they then take hold quite firmly with just one or two turns. It is probably most advantageous to put two screws in each of the major fragments in front and in back of the shattered area, or to use an additional internal wire, in order to secure rigid fixation.

The bar acts as a space retainer, as well as a means of fixation, and it is, therefore, possible to leave some questionable fragments in the shattered area until their viability is finally determined. In one such case, a fairly large separate fragment had been driven down into the soft tissues of the neck, but was replaced and united

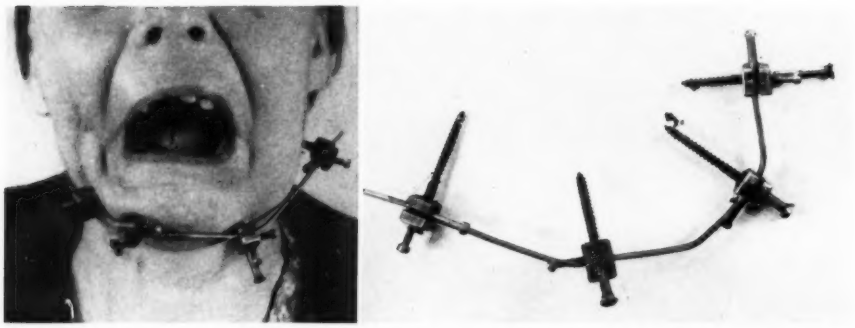


Fig. 10. Open mouth treatment of multiple fractures (4) in edentulous jaw with external bar fixation. Four wood screws directly in fragments. Apparatus removed in 5 weeks, union solid. Lugs designed by Dr. James A. Brown and used on patient of Dr. Louis T. Byars at St. Louis City Hospital.

firmly with the fragments on either side (Fig. 9). In such instances, any soft tissue or periosteal attachments to the fragment should be most carefully preserved. Due to its simplicitv, the external metal bar may be capable of use further forward in war injuries than more complicated methods.

These lugs with set screws for the bone screw and for the external arch, and the screws with compressible slots to hold the external bar have been designed by Dr. James A. Brown, and a more detailed account is to be published.

The internal wire fixation does not require the persistent and close after-care necessary with intricate dental splints, elastic traction, or plaster caps and external traction. In most instances, only 1 or 2 days' hospitalization is sufficient and some patients have returned to work after the first week, reporting for inspection each week or so, or if any unusual symptoms develop. This might be of some value in the postoperative care of mass civilian or military casualties when hospital and surgical facilities might be limited.

# TOTAL GASTRECTOMY

## Technical Considerations

CHARLES BRUCE MORTON, II, M.D., Charlottesville, Virginia

IN a previous report I recorded the cases of four patients subjected to total gastrectomy (8). The technique employed in the last three was so satisfactory that it seemed worth describing in detail and it forms the basis of this report. Concerning technique, it is of interest that the first total gastrectomy recorded was done by Conner in 1884. It resulted fatally for the patient. Schlatter in 1897 removed the entire stomach and his patient survived. As recently as 1933, Roeder found only 88 published instances of the operation. During the past 10 years the operation has been performed much more frequently than before but it is still not commonplace. The indications for total gastrectomy, including suggested liberalization of them, have been discussed in previous communications (8,9) and hence will not be repeated here.

### PREOPERATIVE TREATMENT

It is believed that the treatment the patient receives during the few days preceding operation is one of the most important factors of safety for the operation itself. The first effort is aimed at accurately determining the patient's general physiological status. The next effort is directed toward correction of any abnormality that may have been found. Dehydration, anemia, plasma chloride or protein deficiency, nitrogen retention, cardiovascular renal dysfunction or other serious physiological abnormalities if existent are combatted by appropriate measures. Intravenous administration of solutions of sodium chloride or glucose and of plasma or whole blood is frequently necessary.

This accomplished, the gastrointestinal tract itself is prepared, usually for at least 2 days. The patient with gastric stasis is allowed nothing by mouth, and fluid balance is maintained by solutions of glucose and sodium chloride administered intravenously. Patients without gastric stasis are permitted clear strained liquids by mouth, but in addition receive one intravenous injection of 1000 to 1500 cubic centimeters of glucose or sodium chloride solution each day. In all patients a gastric lavage is administered each night, and preparations are made for at least one or two transfusions of blood (500 c.c. each). During the night before operation some of the barbiturates are employed for sedation, and nothing by mouth is allowed.

On the morning of operation, a small caliber stomach tube is introduced through the nose, passed into the stomach, and attached to a negative pressure apparatus (Fig. 1, insert). It is desirable that this be done at least an hour before the operation. With proper sedation the patient arrives in the operating room in a distinctly drowsy state.

### ANESTHESIA

It is believed that spinal anesthesia is of the utmost importance in facilitating the operation. Pontocain, 20 milligrams dissolved in 4 cubic centimeters of a mixture of equal parts spinal fluid and 5 per cent solution of glucose, injected in the subarachnoid space between the last dorsal and first lumbar vertebrae, has proved ideal. Immediately after the drug is injected the table is tilted, head down, at an angle of about 10 to 15 degrees, until the level of anesthesia, determined by pricking the skin, reaches to just below the nipples. This occurs usually in from 3 to 5 minutes, after which the table is levelled and the anesthesia remains fixed for usually as long as 3 or 4 hours. Continuous spinal anesthesia as described by Lemmon and others might be equally or even more satisfactory but was not tried in the cases comprising this report.

### OPERATION

The technique of the operation was evolved by the study and adaptation of various techniques employed in cases reported by Allen, Lahey, Graham, Walters, and others and by lessons learned through previous experience with subtotal gastrectomy and total gastrectomy. The smooth course of the patients postoperatively indicates that the technique is sound.

In the cases of this report, incision in the middle of the abdomen from the xiphoid to the umbilicus was employed with entire satisfaction and provided excellent exposure. Thorough exploration to determine the extent of gastric invasion and the absence of ineradicable extension

From the Division of Clinical Surgery and Gynecology, University of Virginia.

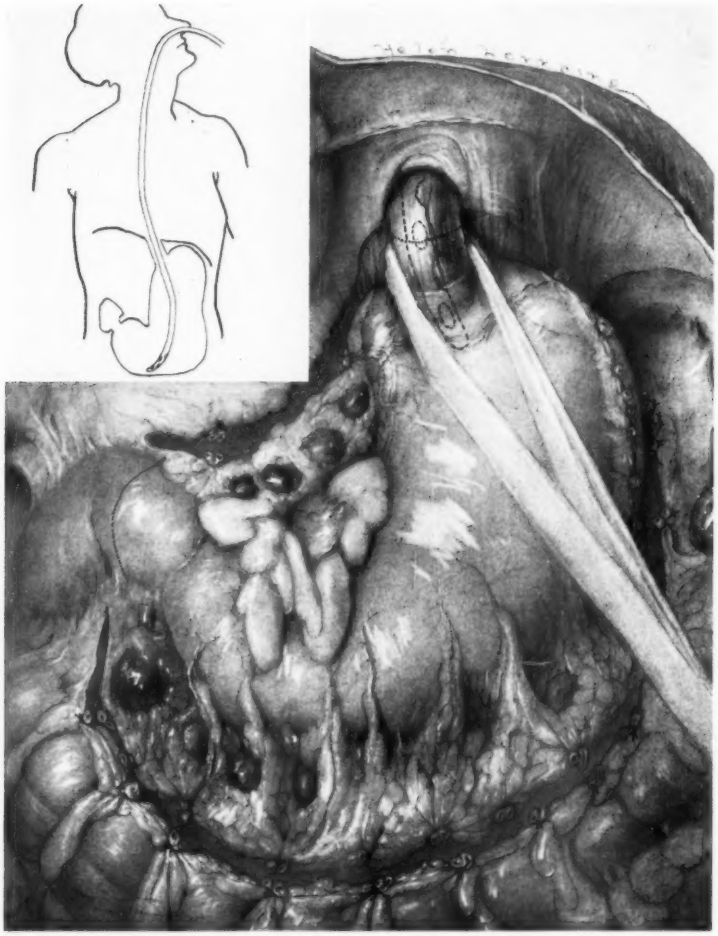


Fig. 1. Exposure of the lower part of the esophagus and the first portion of the duodenum together with complete mobilization of the entire stomach and its contiguous tissues. Insert calls attention to stomach tube passed nasally.

or metastases must be carefully carried out. Provided total gastrectomy seems to offer complete eradication of the tumor, the operation proceeds. During its course the patient's condition is watched carefully and fluids and blood as indicated are introduced intravenously.

With traction on the stomach, the peritoneum on each side of its cardiac orifice is incised and a finger is gently worked around to encircle the esophagus and to permit a tape to be passed around the lower end of the esophagus. In some instances, severance of the peritoneal attachment of the left lobe of the liver to the diaphragm facilitates the exposure. Next the first portion of the duodenum is freed by sharp dissection. Vessels are clamped, sectioned, and ligated with fine silk, first in the gastrocolic and then in the gastrohepatic omentum so that they may be entirely removed with the stomach. The lienogastric vessels are sectioned at the spleen to insure removal of lymph channels and glands found among them. The left gastric vessels are sectioned as close to the celiac axis as possible so that lymphatic tissue in that region may be

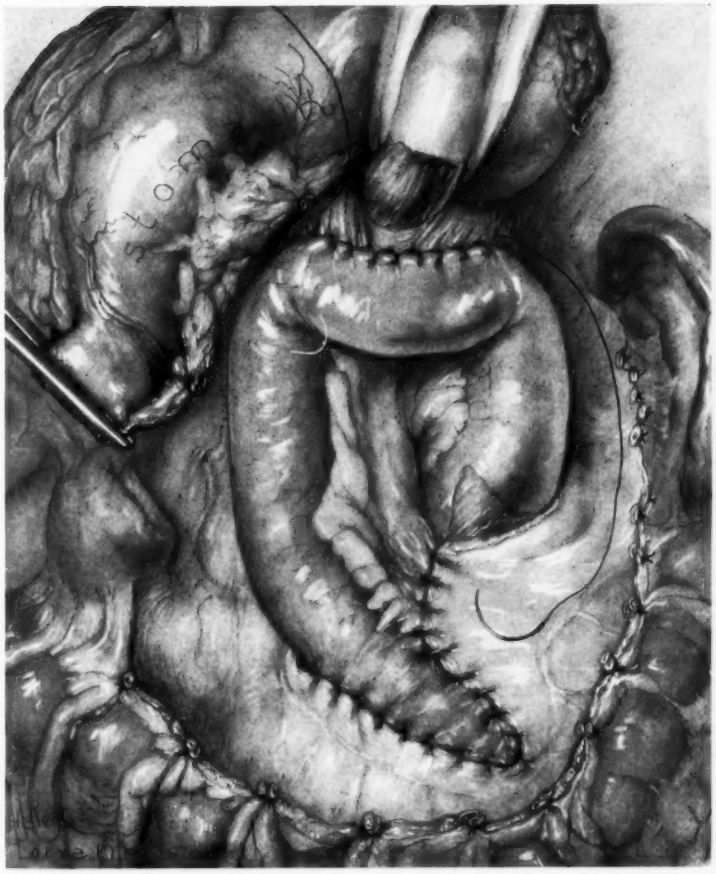


Fig. 2. The duodenum has been sectioned, the distal end closed by suture. The stomach has been reflected upward, thus exposing the posterior aspect of the esophagus. Disposition of the afferent and efferent limbs after suture of the jejunum to the pillars of the diaphragm posteriorly. Note the small denuded area on the afferent loop, representing the point of division of the ligament of Treitz.

radically removed. The stomach now lies entirely free and traction on it will usually pull down a generous part of the lower end of the esophagus and provide surprisingly good exposure (Fig. 1).

A slit is made in the transverse mesocolon, extending down to the ligament of Treitz which is severed so that an appropriate length of the first portion of the jejunum may be brought up for later anastomosis with the esophagus. The slit in the mesocolon is then partly closed by suture with fine silk to the mesentery of the jejunum passing through it and the efferent loop of the jejunum is loosely sutured obliquely through the anterior part of the slit in the mesocolon, thereby closing the remainder of the opening (Fig. 2).

In addition to the usual towels placed to cover the skin margins, the wound edges are covered by infolded laparotomy pads and the intraperitoneal field of operation is carefully isolated in the same manner. The first portion of the duodenum is severed between clamps 2 or 3 centimeters distal to the pylorus, and the distal end is closed by inverting sutures of chromicized catgut and is buried in the head of the pancreas. The stomach is folded upward on the chest and a row of sutures of chromicized catgut is employed to suture the posterior aspect of the peak of the jejunal loop

Fig. 3.

Fig. 4.

Fig. 5.

Fig. 3. Traction sutures increase width of esophagus as the outer posterior row of suture is placed to unite the jejunum and the posterior wall of the esophagus.

Fig. 4. The inner posterior row of suture is progressing to unite the mucosal aspects of the jejunum and the posterior wall of the esophagus.

Fig. 5. The inner anterior row of suture is progressing to unite the mucosal aspects of the jejunum and the anterior wall of the esophagus. Dotted line indicates the last part of the anterior esophageal wall which is to be sectioned and sutured, thus completing the inner anterior row of suture.

to the pillars of the diaphragm behind the esophagus with the efferent loop directed toward the patient's right side (Fig. 2). Allis forceps or traction sutures placed on each side of the cardiac orifice are employed to attain the maximum width of esophagus so that the outside row of chromicized catgut sutures for the end-to-side esophagojejunal anastomosis may be placed posteriorly (Fig. 3). Next a small opening is made in both esophagus and jejunum, and a suture of chromacized catgut, with a small, curved, swaged needle on each end is placed to begin the pos-

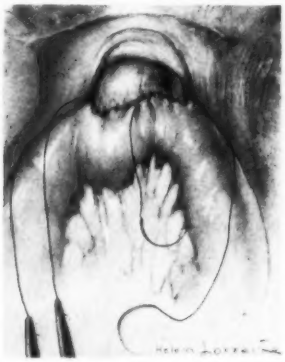


Fig. 6. The outer anterior row of suture, completing esophagojejunal end-to-side anastomosis.

Fig. 7. The final step, suture of the jejunum to the pillars of the diaphragm anteriorly, has completed the operation.

terior part of the inner suture line. At this point in the operation the tube in the esophagus is grasped, withdrawn from the stomach and introduced into the efferent loop of jejunum so that the multiple large perforations in the tube remain at the region of the anastomosis. The other end of the tube, attached to a negative pressure pump, keeps the field of anastomosis dry and clean. As the sutures of the inner row are placed, the openings in both the esophagus and the jejunum are enlarged (Fig. 4) until the entire posterior row is completed. Traction on the still attached stomach keeps the esophagus well down so that suture, while a little tedious, is not difficult. As the anterior suture progresses by the Connell method from each side toward the center, the anterior wall of the esophagus is more nearly severed (Fig. 5) and is finally completely severed as the last suture is placed and the knot tied, completing the anterior part of the inner suture line. The end of the suture employed for the posterior part of the outer suture line is then used to complete the anterior part of the outer suture line (Fig. 6). Finally the end of the suture first used to suture the posterior side of the jejunal loop to the pillars of the diaphragm is continued to suture the anterior side of the jejunal loop to the diaphragm in front of the esophagus (Fig. 7). The suture of the jejunal loop to the diaphragm all around the anastomosis itself relieves the anastomosis of all tension and is an essential feature of the technique.

The anastomosis and the disposition of the jejunum as described leaves the shortest kind of afferent loop, all above the transverse mesocolon, and consequently an equally short efferent loop passing through the mesocolon. By this method there is no logical place for, nor need of, an enteroanastomosis. A jejunostomy tube may be placed lower down in the jejunum for feeding if desired, but it was not used in any of the patients operated upon by this technique.

The incision is closed without drainage of the peritoneum though small, soft rubber drains are placed in the subcutaneous tissue between the stay sutures. These are removed with the skin sutures in from 5 to 7 days.

### POSTOPERATIVE TREATMENT

Postoperative care of the patients is most important. Constantly maintained negative pressure in the tube placed at operation to continually aspirate all fluid material at the site of anastomosis, adequate sedation, use of fluids intravenously, parenteral administration of vitamins, and transfusions of blood are the essential measures. The tube may be removed in from 7 to 10 days, and the next day sips of water by mouth are allowed. During the next 2 or 3 days, the patient fairly rapidly increases the intake of liquid and then soft foods and in about 2 weeks from the time of operation will tolerate a regular five meal type of diet readily. The meals must remain small and frequent for a period of several weeks but soon both the afferent and efferent jejunal loops dilate to form a stomach-like reservoir so that regular and normal size meals are well tolerated. Any tendency toward anemia should be treated with liver extract and vitamins probably should be recommended for a time. Follow-up examination of all patients operated upon by the technique described had demonstrated freedom from digestive symptoms, little or no anemia, excellent general health, a sense of well-being and economic rehabilitation.

### REFERENCES


1. ALLEN, A. W. Am. J. Surg., 1938, 40: 35-41.
2. Idem. Tr. South Surg. Ass., 1937, 50: 165-175; Ann Surg., 1938, 107: 770-780.
3. CONNER, P. S. Med. News, 1884, 45: 578 (Quoted by Allen, 1).
4. EUSTERMAN, G. B., and BALFOUR, D. C. The Stomach and Duodenum. Philadelphia: W. B. Saunders Co., 1935. (Chapter on total gastrectomy by Waltman Walters, pp. 628-635).
5. GRAHAM, R. R. Surgery, 1940, 8: 257-264.
6. LAHEY, F. H. Surg. Gyn. Obst., 1938, 67: 212-223.
7. LEMMON, W. T. Ann. Surg., 1940, 111: 141-144.
8. MORTON, C. B. Arch. Surg., 1942, 44: 72-80.
9. Idem. Surg. Gyn. Obst., 1940, 71: 111-113.
10. ROEDER, C. A. Ann. Surg., 1933, 98: 221-231.
11. SCHLATTER, CARL. Chirurg, 1897, 19: 757 (Quoted by Allen, 1).

# AMYLOID GOITER

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THE occurrence of amyloid deposits in organs other than the liver, kidney, spleen, and adrenal glands is not commonly observed; there is, however, a number of reports of deposits in such unusual places as the heart, lungs, muscles, intestines, lymph glands, and, in fact, almost every organ of the body including the brain. One of the most infrequently involved organs is the thyroid gland, and it is the purpose of this paper to review the literature and to report 2 cases of amyloid infiltration of the thyroid gland.

A search of the literature discloses 56 cases; the cases reported herewith bring the total to 58.

Amyloid deposits in the thyroid gland occurred as a part of the secondary type of amyloidosis in 40 cases, Peters; Schilder; Ipland; Wegelin; Bannick, Berkman, and Beaver; Theodore.

In 3 cases a clinical diagnosis of generalized amyloidosis was made or suspected, and amyloid was found in the thyroid removed surgically from 2 of these (von Eiselsberg; and Toland and Kroger), while amyloid in the thyroid was suspected clinically but not proved in the third, Bannick (1). Thus in 43 cases the lesions were definitely or probably associated with generalized amyloidosis.

The primary disease was pulmonary tuberculosis with or without cavitation or involvement of other organs in 13 cases (von Eiselsberg, Schilder, Ipland, Hunter and Seabrook, Toland and Kroger).

Purulent bronchitis and bronchiectasis were present in 3 cases (Wegelin, Oberling, Theodore).

In 2 instances amyloid was confined to the thyroid gland (Schilder and Oberling).

Neoplastic processes were present in 3 cases, carcinoma or sarcoma in 1 (von Burk), metastatic lymphosarcoma in 1 (von Jacquet), and a carcinoma in the third (Stoffel).

Syphilis and tuberculosis were probably associated in 1 case (von Eiselsberg).

In 4 cases the amyloid in the thyroid was associated with the primary type of amyloidosis (Lubarsch, Strauss).

In 33 cases the associated disease was not reported or not found (Peters; Moritsch; Wegelin; Osgood; Bannick, Berkman, and Beaver; and Bannick).

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Enlargement of the thyroid, true amyloid goiter, was present in 35 cases. In 5 of these the goiter was removed surgically. One patient died 3 days after operation (Oberling), 3 recovered from pressure symptoms (Moritsch; Hunter and Seabrook, Toland and Kroger). One patient was confined to bed after operation because of active pulmonary tuberculosis from which he eventually died (Toland and Kroger, personal communication). One patient developed parathyroid tetany after operation (von Eiselsberg).

## CASE REPORTS

CASE 1. A white male aged 60 years, was admitted to the University of Kansas Hospitals, on the service of Dr. R. H. Major, complaining of goiter, breathlessness, nausea, vomiting, and pain over the umbilicus. He had been well until 15 years prior to admission when a chronic cough with gradually increasing weakness developed. Seven years ago a severe attack of influenza was followed by aggravation of his cough. He was treated for pulmonary tuberculosis at a sanitorium 5 or 6 years ago and returned home, improved. Two or 3 years ago he noticed a tumor in the anterior cervical region which gradually increased in size and was associated with nervousness. For 3 weeks prior to admission he was confined to bed because of breathlessness, weakness, nausea, vomiting, and severe epigastric pain.

Physical examination showed an emaciated patient with pasty complexion. The anterior cervical lymph nodes were enlarged, and there was a tumor in the region of the thyroid which was quite firm and nodular, the size of a grapefruit. The pulse rate was 100 per minute and regular. The blood pressure was 80 systolic and 44 diastolic. Thoracic expansion was limited bilaterally; fine crepitant râles were heard over both apices.

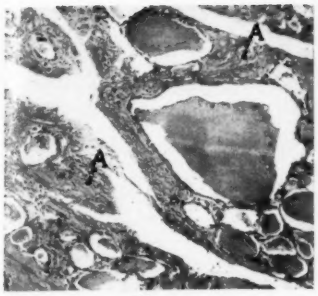
X-ray examination revealed chronic fibrous pulmonary tuberculosis on the right, high diaphragm, and fluid on the left. Laboratory studies showed hemoglobin 53 per cent; nonprotein nitrogen, 100; creatinine, 5.4; albuminuria, 1 plus; urine specific gravity, 1.008. Basal metabolic rate was plus 55 per cent in a single determination.

The clinical diagnosis was pulmonary tuberculosis with nontoxic colloid goiter.

The patient's condition was not considered such as to permit any surgical procedure, chiefly because of breathlessness that was not ameliorated by bed rest. Supportive treatment was given, but the patient became gradually worse and died on the 5th hospital day.

Postmortem examination was done and revealed the following; the body showed considerable emaciation and there was a tumor in the region of the thyroid 7.5 centimeters in transverse diameter projecting forward 5 centimeters.

The right thorax contained 100 cubic centimeters of clear fluid. A few fibrous adhesions were present between the right lung and the pericardium; the right lung was considerably expanded, extending over the midline to the left midclavicular line. The left lung was much reduced in size

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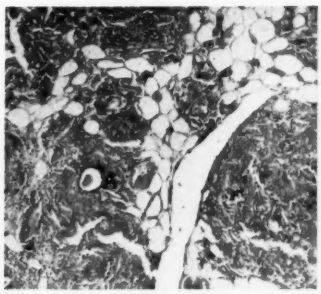


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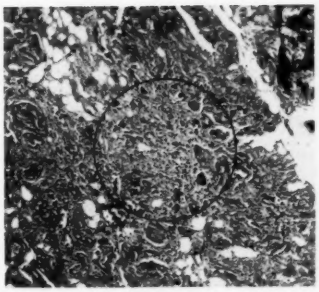

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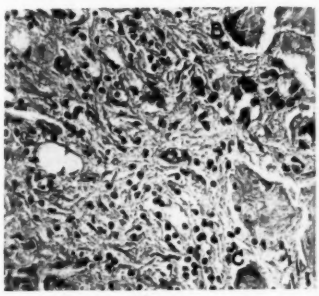


Fig. 4.

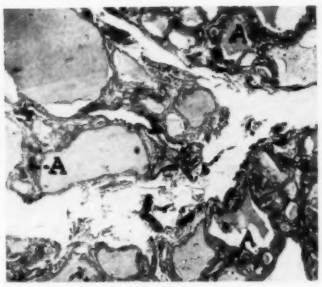


Fig. 5.

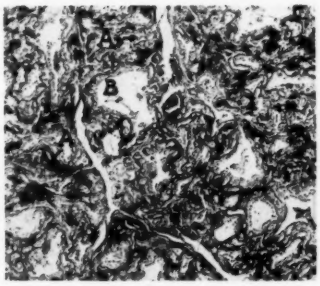


Fig. 6.

Fig. 1. Case 1. Section of the thyroid showing retraction of colloid and follicles in various stages of atrophy. The thick septa *A* are lamina of amyloid. ×55.

Fig. 2. Case 1. Section of thyroid showing almost complete displacement of follicles by lamina of amyloid in the stroma. An atrophic follicle can be recognized at *A*. Note the fat tissue infiltration and scattered mononuclear leucocytes. ×55.

Fig. 3. Case 1. Focal inflammatory lesion consisting of a patch of fibrous tissue infiltrated with mononuclear cells and a few giant cells. ×55.

Fig. 4. Case 1. High power of the area outlined in Figure 3. Note the multinucleated giant cells at *B* and *C*. These did not contain amyloid. The lesion is obviously not a tubercle and apparently represents a reaction to the amyloid present. ×55.

Fig. 5. Case 2. Section of thyroid showing colloid filled follicles separated by lamina of amyloid at *A*. ×55.

Fig. 6. Case 2. Section of the thyroid showing extensive infiltration of the stroma with amyloid at *A*. Note at *B* the atrophic follicles, some of which contain irregular shrunken masses of colloid. ×85.

and was completely adherent to the chest wall except posteriorly where a thick walled empyema cavity containing 100 cubic centimeters of pus was found. The mediastinum was displaced to the left. There was bronchiectasis, interstitial pneumonitis, emphysema, and tuberculous bronchopneumonia of the right lung. The left lung also showed irregular fibrosis and a few areas of caseation. Fibrinous pleurisy was present on the right.

The kidneys were small (70 grams each) and somewhat flabby. The cut surface was mottled with fine yellow dots in both cortex and medulla, the glomeruli could not be made out and the pelves were moderately distended.

The wall of the cecum was thin, and the mucosa ulcerated, the ulcers showing slight induration and being oriented transversely.

The appendix was obliterated distally.

The thyroid gland weighed 280 grams and measured 10 by 8 by 6 centimeters in size. It was moderately firm in consistency and coarsely lobulated. The cut surface had a homogeneous appearance and a yellow color but was not greasy, nor did it present the waxy appearance usual for amyloid-containing organs. Irregular lobulations could be made out but no colloid could be recognized. Application of Lugol's solution to the cut surface resulted in a typical mahogany brown color reaction characteristic of amyloid.

The trachea showed compression with narrowing of the lumen just below the thyroid cartilage, the tracheal rings at this point were softened and displaced toward the left.

The histological findings were:

The arterioles of the myocardium showed abundant deposits of amyloid in the intima. Moderate perivascular fibrosis was present, and the endocardium was irregularly thickened.

The lungs showed organizing acute fibrinous pleurisy, dilated bronchi with desquamated epithelium and peribronchial round cell infiltration, areas of diffuse fibrosis and thickening of the framework with considerable chronic inflammatory reaction, extensive areas of atelectasis and caseous bronchopneumonia with a few giant cells and granulomatous foci. Many arterioles showed great thickening of the wall with deposits of amyloid in the intima.

The liver showed capsular thickening with periportal fibrosis and congestion of the central zone with some atrophy and necrosis. Many of the arterioles showed deposits of amyloid in the intima.

The spleen showed amyloid in the intima of the arterioles and small amounts of amyloid in the malpighian bodies. No amyloid was seen in the pulp.

The intima of the arterioles in the adrenal glands contained amyloid, and there were a few scattered mononuclear cells in the medulla.

The kidneys showed extensive diffuse fibrosis of the cortex and medulla with marked degeneration of the convoluted tubules and diffuse chronic inflammatory reaction. Nearly every glomerulus showed some deposit of amyloid, the majority being largely replaced by this material which was also present in the intima of many of the smaller arteries and arterioles. Many of the surviving convoluted tubules were dilated, contained hyaline and amyloid casts and numerous polymorphonuclears in some instances. Irregular masses of amyloid were present in the stroma of the medulla.

The wall of the cecum showed ulceration, chronic inflammatory granulation tissue, and a few focal granulomatous lesions but no definite tubercles.

The capsule of the thyroid was not thickened. The lobulation was unusually distinct. The usual colloid-containing follicles were almost completely absent, the bulk of the organ consisting of extensive masses of amyloid material having in some areas a fibrillar structure suggesting the appearance of hyaline fibrous tissue. Numerous islands of fat cells were intermingled with the amyloid, and in some sections the amount of fat tissue was approximately as great as that of the amyloid. Occasionally thyroid follicles containing colloid could be recognized. In some instances the follicles were cystic, lined by cuboidal epithelium, and contained nothing but a few desquamated epithelial cells. These cystic follicles rested directly in contact with the amyloid in the adjacent stroma and in some instances amyloid appeared in the basement membrane which was considerably thickened thereby. In most sections the follicles were reduced to narrow cleft-like spaces usually without epithelial lining although a few degenerated epithelial cells could occasionally be recognized. In areas not so heavily infiltrated with amyloid the capillaries showed a ring of this material forming a sort of basement membrane for the endothelium which was swollen and showed some tendency to proliferation. Isolated multinucleated giant cells, occurring singly or in small groups (Figs. 3 and 4) were fairly frequently seen. Phagocytosis of amyloid could not be demonstrated. There were also scattered focal accumulations of lymphoid cells lying in the looser meshed connective tissue and fat tissue in various sections (Fig. 2).

The perivascular and perifollicular location of the early amyloid deposits suggested that the material had first made its appearance between the endothelium of the capillaries and the basement membrane of the follicles, and that, as the amount of amyloid increased, there had been a gradual compression of the follicles with resorption of the colloid and atrophy of the epithelium, ultimately resulting in almost complete replacement of the parenchyma by amyloid.

Application of Lugol's solution to the gross material and staining of the microscopic preparations with congo red and methyl violet gave the typical staining reactions for amyloid in the thyroid, kidney, adrenal glands, arterioles of the heart, spleen, lungs, liver, and pancreas. Staining with sudan III demonstrated considerable amounts of fat tissue in the thyroid and fat droplets in the convoluted tubules of the kidney.

The final anatomical diagnosis was: chronic bronchiectasis (tuberculous?), chronic interstitial pneumonitis, left atelectasis, compensatory right emphysema, tuberculous bronchopneumonia, encysted empyema, acute fibrinous pleurisy, right hydrothorax; generalized amyloidosis with particular involvement of the thyroid gland, kidneys, spleen and the arterioles of the heart, lungs, liver, and pancreas; chronic ulcerative colitis, edema of the liver, chronic thyroiditis with extensive lipomatosis; generalized arteriosclerosis, coronary sclerosis, chronic myocarditis, hypertrophy and dilatation of the heart, chronic passive congestion of the liver and kidneys, right inguinal hernia, anthracosis, obliterating appendicitis.

CASE 2. A white male, aged 16 years, was admitted to the University of Kansas Hospitals on the service of Dr. S. H. Snider, complaining of tuberculosis. One year prior to admission he had noted weakness, dyspnea, fever, and cough with increased expectoration. Acid fast bacilli were found in the sputum and the patient was put to bed. Somewhat later the family changed physicians, and the new attendant allowed the patient to resume ordinary activities, stating that he "might" have a goiter and that the pulse was too rapid.

Two weeks prior to admission the patient attended the out patient clinic of the University of Kansas Hospitals where a diagnosis of far advanced pulmonary tuberculosis was made on the basis of x-ray findings and the presence of tubercle bacilli in the sputum.

Physical examination on admission showed a pale emaciated individual with atrophy of the left upper thoracic and supraclavicular muscles, and numerous moist rales over the upper chest bilaterally. The heart rate was 94; blood pressure, 90 systolic and 50 diastolic; weight, 93 pounds.

X-ray study revealed active bilateral tuberculosis of the lungs with cavitation.

The progress after admission was slowly but inexorably downward. Sixteen months after admission vomiting after meals or a paroxysm of coughing developed and was later associated with abdominal distress, distention, and tenderness. A diagnosis of tuberculous enteritis was made at this time and pneumoperitoneum was instituted. This was maintained for many months without any improvement of symptoms. Seventeen months after admission the right phrenic nerve was crushed, but this did not result in any tendency to healing in the right lung. Twenty-two months after admission laryngeal symptoms appeared and hoarseness was very marked. A mass was palpated in the upper abdomen on the left, and fluid was detected in the abdomen 41 months after admission. Albuminuria developed at about the same time and shortly thereafter intravenous injection of congo red revealed 95 to 100 per cent retention of the dye after 1 hour. Icterus developed at this time, and repeated abdominal paracentesis yielded approximately 25 liters of fluid over a period of 2 months.

Death occurred 44 months after the patient's admission to the hospital.

The final clinical diagnosis was pulmonary tuberculosis with cavitation, tuberculous enteritis and peritonitis, tuberculous laryngitis, generalized amyloidosis due to tuberculosis.

At postmortem examination the following data were obtained:

The body weighed 75 pounds and measured 5 feet 10 inches in length.

The pleural cavities showed complete synechia. There were bilateral tuberculous lesions of the bronchogenic type with multiple cavities, tuberculous hilar lymphadenitis, tuberculous enteritis and peritonitis, tuberculosis of the adrenal glands.

The liver and spleen were enlarged, firm, and rubbery in consistency and mottled orange in color; the adrenal glands showed the same mottled coloring but were not enlarged or hard.

The thyroid gland was not enlarged (weight 10 grams), it was light reddish brown in color, firm in consistency, and the cut surface showed a homogeneous appearance; no colloid could be recognized.

The orange red mottling of the liver, spleen, and adrenal glands and the reddish brown color of the thyroid were apparently due to congo red staining of the amyloid in these organs as a result of intravenous administration of the dye during life.

The results of histological examination were:

Amyloid deposits were found consistently in the stroma, frequently in the intima of the arterioles, and occasionally in the venules of the heart, lungs, liver, spleen, adrenals, kidneys, pancreas, small intestine, prostate, many lymph glands and the omentum. Hyperplastic fibrous tuberculous lesions were present in the lymph glands, lungs, and adrenals, and a few tuberculous cavities were seen in the lungs.

A few areas of fat necrosis with moderate acute inflammatory reaction were present in the pancreas.

The vocal cords showed bilateral tuberculosis.

The capsule of the thyroid was not thickened, the lobulation was unusually distinct. The stroma of the gland was extensively infiltrated with amyloid. In most areas the follicles were atrophic and lined with cuboidal or low columnar epithelium showing a tendency to desquamation. The colloid presented a variable appearance, being smooth and homogeneous in some follicles while in others it was granular, greatly retracted, and sometimes vacuolated. Few follicles remained in most fields and these were reduced to cleft-like spaces with degenerated lining cells. The bulk of the gland consisted of amyloid material having a fibrillar structure much like hyaline fibrous tissue. The capillaries were very difficult to identify because of their resemblance to the numerous clefts in the section; the endothelium was poorly defined and appeared degenerated. Amyloid was present in the intima of many arterioles. There was no lipomatosis in this gland and no evidence of an inflammatory process was found.

The final anatomical diagnosis was: chronic pulmonary tuberculosis with cavitation, tuberculous laryngitis with ulceration, tuberculous enteritis, omentitis, lymphadenitis and chronic adhesive pleurisy with complete synechia, chronic adhesive perihepatitis and perisplenitis; generalized amyloidosis with particular involvement of the liver, spleen, pancreas, adrenal glands, kidneys, lungs, heart, intestine (colon), prostate, lymph glands, small intestine, omentum and thyroid gland. Emaciation, acute dilatation of the heart. Decubitus ulcers, accessory spleen, fat necrosis of the pancreas.

The response to application of Lugol's solution to the gross and methyl violet to the histological preparations was in every way typical for amyloid.

In 1893 Wichmann classified amyloid disease into generalized and localized forms. In 1929 Lubarsch recognized an essential difference between various forms and grouped them into typical or generalized and atypical or systematized forms. Since this paper appeared many other terms have been introduced. Thus such terms as typical, genuine, classical, visceral, generalized, orthochromatic, pericapillary and periglandular have been applied to the form of amyloid disease which is often associated with some chronic illness. The atypical form has been designated as primary, unusual, idiopathic, systematized, paramyloidosis, etc. Reimann, Koucky, and Eklund in 1935 discussed the various terms here mentioned and suggested a simple clinicopathological classification into 4 groups; primary amyloidosis, tumor forming amyloid disease, secondary amyloidosis, and amyloidosis with multiple myeloma.

The cases reported herewith are obviously examples of the secondary type of amyloidosis, unusual in that the thyroid gland showed extensive deposits.

In none of the reported cases was there any evidence of thyroid insufficiency, on the contrary, the first case reported herewith had an elevated basal metabolic rate, probably due to dyspnea.

In the first case here described amyloid infiltration of the thyroid was associated with lipomatosis as well. In view of the fact that the thyroid is an organ in which fat tissue is extremely rare, this finding would suggest that there may be some more than casual relationship between the two conditions. That this is possible is supported by the fact that a search of the literature reveals several other examples in which amyloid infiltration has been asociated with lipomatosis. Thus Virchow mentioned the observation of fat tissue in the stroma of a thyroid containing amyloid in some fetal adenomas. (This case is not discussed specifically but is included among the 10 cases discussed by Peters.) Ecoffey found fat tissue in the center of an amyloid tumor of the larynx; Oberling found much fat in the thyroid of his case of amyloid goiter, and he mentioned a similar finding in an amyloid tumor of the larynx and in the adrenals. These examples could no doubt be added to by a more minute search of the literature but it seems clear that the concomitant occurrence of lipomatosis and amyloid infiltration is probably more than a mere coincidence, although it must be admitted that fat tissue is by no means always a part of the picture of amyloidosis.

## SUMMARY AND CONCLUSIONS

The literature of amyloid goiter contains reports of 56 cases. Two additional cases reported herewith bring the total to 58. The classification of amyloid disease suggested by Reimann, Koucky, and Eklund is accepted, and the cases reported are placed in the secondary type of that classification.

The following conclusions have been made:

1. The commonest primary disease associated with amyloid infiltration of the thyroid is pulmonary tuberculosis. Purulent bronchitis with bronchiectasis or neoplastic processes are less commonly the precursors.

2. Amyloid infiltration of the thyroid may occur as a part of a primary amyloidosis.

3. Amyloid infiltration of the thyroid without amyloid in any other organ is a very rare phenomenon, only 2 cases being found in the literature (Schilder, Oberling).

4. Amyloid infiltration of the thyroid gland causes enlargement and increase in consistency in the majority of cases but does not invariably do so.

5. Amyloid infiltration of the thyroid is sometimes associated with striking fat tissue infiltration as well. The possibility that this is more than a casual relationship is discussed.

6. In no case of thyroid amyloidosis reported has there been any evidence of insufficiency.

7. The most common error in diagnosis is to conclude that a malignancy is present when actually amyloid is responsible for enlargement and increase in consistency as well as nodularity of the thyroid. On the other hand amyloid may cause considerable enlargement of the thyroid without any change in consistency.

## REFERENCES


1. Bannick, E. G. Med. Clin. N. America, 1934, Sept., pp. 413–418.
2. Bannick, E. G., Berkman, J. M., and Beaver, D. C. Arch. Int. M., 1933, 51: 978–990.
3. Burk, U. von. Ueber einen amyloid Tumor mit Metastasen. Inaug. Diss. Tubingen, 1901.
4. Ecoffey. Degenerescence amyloids du poumon. Paris: G. Doin 1924. Cited by Oberling (11).
5. Eiselsberg, F., von. Arch. klin. Chir., 1904, 7: 649–655.
6. Hunter, W. C., and Seabrook, D. B. Arch. Surg., 1930, 20: 762–766.
7. Ipland, H. Frankf. Zschr. Path., 1915, 16: 441–455.
8. Jacquet, von. Virchows Arch., 1906, 185: 251–260.
9. Lubarsch, O. Virchows Arch., 1929, 271: 867–889.
10. Moritsch, P. Deut. Zschr. Chir., 1925, 191: 361–360.
11. Oberling, C. Ann. anat. path., 1927, 4: 125–131.
12. Osgood, E. E. Personal communication to Hunter and Seabrook (6).
13. Peters, W. Ein Fall von amyloider Degeneration der Schilddruse. Inaug. Diss. Freiburg im Breisgau, 1888. Cited by Wegelin (22).
14. Reimann, H. A., Koucky, R. F., and Eklund, C. M. Am. J. Path., 1935, 11: 977–987.
15. Schilder, P. Beitr. path. Anat., 1909, 46: 602–634.
16. Schonof, S. Frankf. Zschr. Path., 1913, 12: 157–165.
17. Stoffel, E. Virchows Arch., 1910, 201: 245–251.
18. Strauss, A. Virchows Arch., 1933, 291: 219–236.
19. Theodore, F. H. J. Mount Sinai Hosp. N. York, 1934, 1: 117–120.
20. Toland, C. G., and Kroger, W. P. West. J. Surg. 1931, 39: 372–374.
21. Virchow, R. Cited by Oberling (11). Geschwulste, 1862, 3: 83–85. Berlin: A. Hirschwald, 1863, 1867.
22. Wegelin, C. Amyloidosis der Schilddruse. Handbuch der speziellen pathologischen Anatomie und Histologie. Henke und Lubarsch. Bd. 8 p. 95. Berlin: Julius Springer, 1926.
23. Wichman, G. Beitr. path. Anat., 1893, 13: 487–628.

# THE ESTROGEN SPARING EFFECT OF HYSTERECTOMY

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THAT hysterectomy is followed by changes in the remaining genital organs has been demonstrated in the rabbit (2, 24) as well as in the guinea pig (22, 23) and the rat (3). Some of these effects in the rabbit and rat are prevented by transplantation of the uterus (13, 35), so that it seems clear that the mechanism is an hormonic one. The most striking effect of hysterectomy in these animals is the prolongation of the life of the corpus luteum, and the changes in the other organs, notably the mammary gland, are due primarily to its continued function. Another experimental technique by which the corpora lutea may be maintained in a functional state beyond the usual time in the rabbit both in pseudopregnancy (1, 39) and in pregnancy (15) is the injection of estrogenic hormone. Since estrogen produced in the growing ovarian follicle is essential in the rabbit for the normal development and maintenance of the corpora lutea (37, 41), these two observations may be correlated if one supposes that the uterus, dependent as it is on estrogenic hormone for its growth and maintenance, uses it up. When the uterus is removed, less estrogen is used, there is more estrogenic hormone available, and the life of the corpora lutea is prolonged just as it is when estrogen is injected.

To test this hypothesis, experiments were devised to determine the effect of partial hysterectomy on the survival of the corpora lutea in pseudopregnant rabbits, and the effect of the injection of estrogen in intact and partially hysterectomized animals. For if estrogen is spared by total hysterectomy, it should also be spared, but to a lesser extent, if part of the uterus is removed, and since the corpora lutea can be prolonged beyond the usual time by the injection of estrogenic hormone, a dose of estrogen which would just fail to maintain them with the uterus intact, might be expected to prolong their function with part of the uterus removed. As is the case with any endocrine gland, function of the corpora lutea cannot be perfectly correlated with their histological appearance. Therefore, several reactions known to be dependent on the function of the corpus luteum, *progestin effects*, were used to determine the state of the corpora lutea.

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## CRITERIA FOR DETERMINING FUNCTION OF THE CORPORA LUTEA

*1. The gross and microscopic appearance of the corpora lutea.* At about the 16th day of pseudopregnancy in the rabbit, the corpora lutea begin to degenerate. They become pale and decrease in size. Histologically many of the lutein cells are smaller and their nuclei are pycnotic. These cells stain more deeply with eosin, so that the corpus luteum has a mottled appearance under the low power magnification. Vacuolization is more widespread and the vacuoles are larger than those seen in lutein cells at the height of their function. There is an irregular increase in connective tissue throughout the corpora lutea and infiltration of wandering cells of varying degree.

These changes in the corpora lutea of the rabbit following pseudopregnancy have been described in detail and compared with the changes which occur after total or nearly total hysterectomy by Loeb and Smith (24). Degenerative changes, although similar, occur much later in hysterectomized animals. Even at 50 days the remnants of the corpora are larger in hysterectomized animals than in intact animals. The preservation of the corpora lutea in totally hysterectomized animals is shown by rabbit Y 345, Table II. There were no more signs of degeneration in the corpora at 26 days than may be seen at 12 days in the intact animal.

TABLE I.—ANIMALS WITHOUT CORPORA LUTEA GIVEN ESTROGEN

| Rabbit number | Daily dose of estradiol benzoate—rat units* | Day mated (from beginning of treatment) | Day examined (from beginning of treatment) | Ovulation | Reaction of uterus *in vitro* to pituitrin | Progestin effect in endometrium |
|---|---|---|---|---|---|---|
| **Estrus Animals** | | | | | | |
| Y 418 | 40 to 160 | 19 | 20 | No | C++ | None |
| Y 419 | 40 to 160 | 19 | 20 | Yes | C++ | None |
| **Castrated Animals** | | | | | | |
| X 987 | 20 | — | 16<br>21 | —<br>— | C++<br>C++ | None<br>None |
| X 988 | 20 | — | 16<br>21 | — | C++<br>C++ | None<br>None |
| Y 417 | 40 to 160 | Mating refused days 18 and 23 | 23 | — | C++ | None |

*6000 rat units=1 mgm.

TABLE II.—PSEUDOPREGNANT ANIMALS WITH VARYING AMOUNTS OF THE UTERUS REMOVED

| Rabbit number | Estimated amounts of uterus remaining | Day mated | Day examined | Ovulation | Reaction of uterus *in vitro* to pituitrin | Microscopic appearance of corpora lutea | Progestin effect in endometrium |
|---|---|---|---|---|---|---|---|
| Y 345 | 0 | — | 26* | — | — | Well preserved | — |
| | | Mating refused | 50 | — | — | Extreme degeneration | — |
| Y 369 | 1/10 | — | 21 | — | N | Beginning degeneration | None |
| Y 418 | 1/8 | 28 | 29 | Yes | N | Beginning degeneration | None |
| Y 436 | 22% | 28 | 29 | Yes | N | Advanced degeneration | None |
| Y 373 | 1/4 | — | 21 | — | N | Advanced degeneration | None |
| Y 363 | 1/4 | Mating refused | 18 | — | N | Well preserved | Slight surface change |
| Y 438 | 24% | 28 | 29 | Yes | N | Extreme degeneration | None |
| Y 366 | 1/4 | Mating refused | 19 | — | N | Advanced degeneration | None |
| Y 434 | 28% | Mating refused | 29 | — | C++ | Extreme degeneration | None |
| Y 415 | 1/3 | 21 | 22 | Yes | C++ | — | — |
| Y 435 | 42% | 28 | 29 | Yes | C+ | Extreme degeneration | None |
| Y 389 | 1/2 | Mating refused | 21 | — | C++ | Advanced degeneration | None |
| Y 365 | 1/2 | — | 18 | — | N | Generally well preserved | Slight surface change |
| Y 36 | 5/6 | — | 21* | — | C++ | Beginning degeneration | None |
| | 1/2 | 26 | 26 | — | R+ | Beginning degeneration | Moderate progestational proliferation |
| Y 342 | all | — | 18* | — | C++ | Well preserved | Slight surface change |
| | 5/6 | — | 28 | — | C++ | Extreme degeneration | None |

*One ovary was removed at this time

With adequate dosage of estrogenic hormone, degeneration of the corpora lutea can be prevented in pseudopregnant rabbits with intact uteri for more than twice the usual life span of the corpora. For example, the corpora of Y 143 and Y 144, Table III, showed no signs of degeneration at 35 days.

In the tables, the appearance of the corpora lutea by histological examination are indicated by the following: well preserved, when no signs of degeneration are seen; generally well preserved, when signs of degeneration appear only in limited areas; beginning degeneration, when there are early signs of degeneration throughout; advanced degeneration, when there is degeneration throughout with some shrinking of the corpora lutea; and extreme degeneration when there are advanced degenerative changes with marked shrinking of the corpora.

*2. The histological appearance of the endometrium:* The progestational proliferation (transformation) of the endometrium regresses after about the 15th day in pseudopregnancy, and by the 21st day has usually returned to the condition of estrus. A change in the surface epithelium of the endometrium is sometimes seen to a slight extent in late pseudopregnancy. It consists of an apparent fusing of the cytoplasm of the superficial cells forming what appear to be large giant cells, which are subsequently shed into the lumen. During pregnancy in the sterile uterine horn of rabbits pregnant in one horn of the uterus, the process becomes extensive. The superficial cells become fused over large areas and form a sort of syncytium lining the lumen of the uterus (Fig. 1, a). This change occurs in castrated rabbits treated with both estrogenic hormone and progesterone over long periods. It has been de-

TABLE III.—PSEUDOPREGNANT ANIMALS WITH UTERUS INTACT, GIVEN ESTROGEN

| Rabbit Number | Daily dose of estradiol benzoate—rat units | Day injections began | Day mated | Day examined | Ovulation | Reaction of uterus *in vitro* to pituitrin | Microscopic appearance of corpora lutea | Progestin effect in endometrium | Weight of uterus—grams | Number of corpora lutea | Weight of animals—grams |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Y 380 | 20 to 40 | 11 | Mating refused | 22 | — | C++ | — | None | — | — | — |
| Y 383 | 60 | 11 | —<br>22 | 21<br>26 | —<br>Yes | C++ | — | None | — | — | 3240 |
| Y 396 | 20 to 80 | 13 | 28 | 29 | No | C++ | Beginning degeneration | Slight perivascular change | — | — | 4740 |
| Y 402 | 20 to 80 | 11 | 29 | 30 | Yes | C++ | Extreme degeneration | None | — | — | 3333 |
| Y 413 | 20 to 80 | 11 | 28 | 29 | Yes | C++ | Extreme degeneration | None | 8.7 | 5 | 2620 |
| Y 414 | 20 to 80 | 11 | 28 | 29 | No | C++ | Generally well preserved | Perivascular change | 5.1 | 6 | 3060 |
| Y 356* | 20 to 80 | 12 | 28 | 29 | No | N | Well preserved | None | 11.6 | 7 | 3920 |
| Y 376* | 20 to 80 | 12 | 28 | 29 | Yes | C+ | Advanced degeneration | None | 25.4 | 10 | 5420 |
| Y 417 | 20 to 80 | 11 | Mating refused | 29 | — | C+— | Well preserved | Slight surface change | 8.4 | 11 | 3000 |
| Y 404 | 40 to 160 | 11 | Mating refused | 29 | — | C++ | Advanced degeneration | Perivascular change | 2.5 cm. segment 2 | 9 | 3920 |
| Y 405 | 40 to 160 | 11 | 28 | 29 | No | R+ | Generally well preserved | Some progestational proliferation, perivascular change and necrosis | 2.5 cm. segment 1.4 | 11 | 3560 |
| Y 408 | 40 to 160 | 11 | 28 | 30 | No | C++ | Beginning degeneration | Perivascular change; necrosis | 9.9 | 6 | 2650 |
| Y 409 | 40 to 160 | 11 | 29 | 30 | No | C++ | Beginning degeneration | Perivascular change; necrosis | 8.5 | 7 | 3030 |
| Y 411 | 40 to 160 | 11 | 28 | 29 | Yes | C++ | Advanced degeneration | Perivascular change | 10.7 | ? 4 | 3530 |
| Y 143 | 20 to 400 | 11 | — | 35 | — | — | Well preserved | Perivascular change; necrosis, extensive | — | — | 5240 |
| Y 144 | 20 to 400 | 11 | — | 35 | — | — | Well preserved | Surface change | — | — | 4030 |

*One ovary previously removed.

scribed by Loeb in association with deciduomata in the rabbit (21) and it is seen when the life of the corpora lutea has been prolonged by estrogen (4). It does not occur in the absence of the corpora lutea unless progestin has been injected. Its presence, therefore, is evidence of corpus luteum function.

The appearance of the endometrium is variable in animals whose corpora have been maintained anatomically beyond the usual time of pseudopregnancy (39). The endometrium may be in the estrus condition or it may show varying degrees of progestational proliferation. If large enough doses of estrogen are given, necrosis involving the muscle as well as the endometrium is produced. The necrosis is always seen in association with the perivascular change, a decidua-like reaction occurring in the cells of the tunica muscularis of the arterioles of the lamina propria of the mucosa and the muscularis of the uterus (Fig. 1, c, d). It consists of enlargement of the cells with vacuolization and rarefaction. In extreme cases it seems also to involve the smooth muscle of the uterine wall in association with necrosis. With somewhat smaller doses of estrogen the perivascular change is seen in the absence of any necrosis. These changes do not appear in animals without corpora lutea, that is, estrus animals or castrates injected with estrogen, Table I, but they are seen in castrated animals injected with

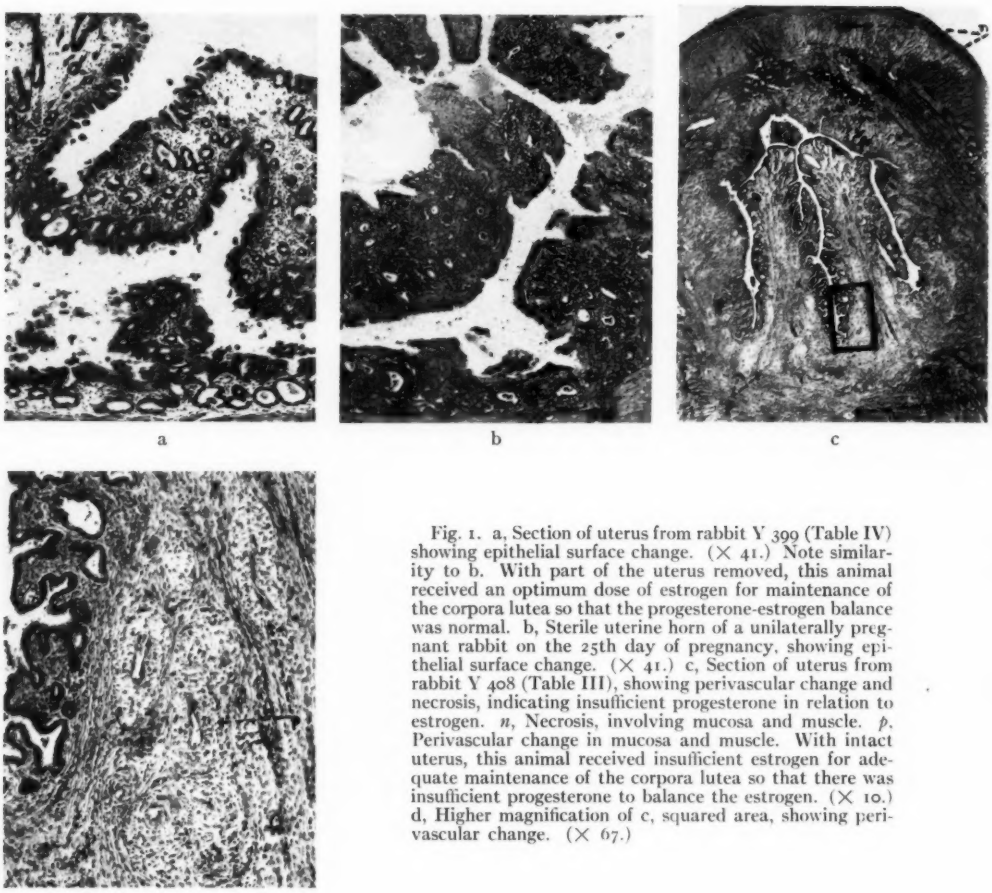

Fig. 1. a, Section of uterus from rabbit Y 399 (Table IV) showing epithelial surface change. (× 41.) Note similarity to b. With part of the uterus removed, this animal received an optimum dose of estrogen for maintenance of the corpora lutea so that the progesterone-estrogen balance was normal. b, Sterile uterine horn of a unilaterally pregnant rabbit on the 25th day of pregnancy, showing epithelial surface change. (× 41.) c, Section of uterus from rabbit Y 408 (Table III), showing perivascular change and necrosis, indicating insufficient progesterone in relation to estrogen. *n*, Necrosis, involving mucosa and muscle. *p*, Perivascular change in mucosa and muscle. With intact uterus, this animal received insufficient estrogen for adequate maintenance of the corpora lutea so that there was insufficient progesterone to balance the estrogen. (× 10.) d, Higher magnification of c, squared area, showing perivascular change. (× 67.)

both estrogen and progesterone in which the amount of estrogen has been too great for the production of the epithelial surface change of late pregnancy. They indicate, therefore, an amount of estrogen which is excessive in relation to progesterone.

*3. The reaction of the uterine muscle to pituitrin in vitro.* A piece of rabbit's uterus suspended in Ringer-Locke solution contracts when pituitrin is added to the bath if the animal has been in estrus, but during pseudopregnancy or the early part of pregnancy, the muscle is refractory to pituitrin (17–20). It either fails to respond or relaxes. The failure of the uterus to contract to pituitrin is due to the presence of corpora lutea in the ovaries. It has further been shown by injecting estrogen and progesterone in castrated rabbits that progesterone is responsible for the failure of the uterus to contract when pituitrin is added to the bath (4, 14). There are three types of reaction to pituitrin: (1) contraction; (2) no response, in which the pattern of the spontaneous contractions is not disturbed; and (3) relaxation of varying degree. In general, relaxation is seen when the function of the corpora lutea is most active, as judged by the microscopic appearance of the endometrium and of the corpora lutea in pseudopregnancy and pregnancy, that is, from the 6th to the 15th day in pseudopregnancy and from the 6th to 25th day in pregnancy, Figure 2, *1*, *5*. In castrated rabbits given both hormones, relaxation is seen when the endometrium shows changes like those of pregnancy (sterile horn). These changes are progestational proliferation and later,

if the injections are continued, surface change. If the amount of estrogen is excessive in relation to progesterone, the uterus contracts to pituitrin, and this may be seen in association with the perivascular change and necrosis.

*4. The occurrence or non-occurrence of ovulation after mating.* Ovulation in the rabbit does not occur during pseudopregnancy because of the presence of corpora lutea in the ovaries (11). That progesterone is responsible for this inhibition has been shown (26). Estrogenic hormone alone does not inhibit ovulation (30).

## THE EXPERIMENTS

The experiments fall into three groups: (1) Pseudopregnant animals with varying amounts of the uterus removed were examined at various times after the 16th day. The purpose of these experiments was to determine whether partial hysterectomy tends to prolong the life of the corpus luteum. It has been stated to do so in the guinea pig (22, 23). If the theory be correct that removal of the uterus results in maintenance of the corpora lutea because estrogen is thereby spared, this may occur, for partial hysterectomy might be expected to have the same effect as injection of estrogen. (2) Pseudopregnant animals with the uterus intact, and others with part of the uterus removed were given similar doses of estrogen. If the uterus uses estrogen, removal of part of it should result in a decrease in the amount used and should increase the effectiveness of injected estrogen in prolonging the life of the corpora lutea. A dose of estrogen, then, just too small to maintain the corpora lutea in animals with the uterus intact, should maintain them in partially hysterectomized animals. (3) Pseudopregnant animals with intact uteri were given a dose of estrogen inadequate to maintain the corpora lutea and then these same animals, after part of the uterus had been removed, were given the same or a smaller dose of estrogen during a second pseudopregnancy. The subminimal dose of estrogen with the uterus intact should be sufficient to maintain corpora lutea with part of uterus removed.

Sexually mature rabbits kept in separate cages were used in the experiments. Ovulation was induced by mating or by the injection of pregnancy urine. The occurrence of ovulation was checked the following day by laparotomy at which time the tubes were tied off, if ovulation had been induced by mating. If part of the uterus was to be removed, it was done at this time. At the termination of the experiments, uterus and ovaries were fixed in Zenker's solution and formalin and sectioned. The uteri with the mesometrium

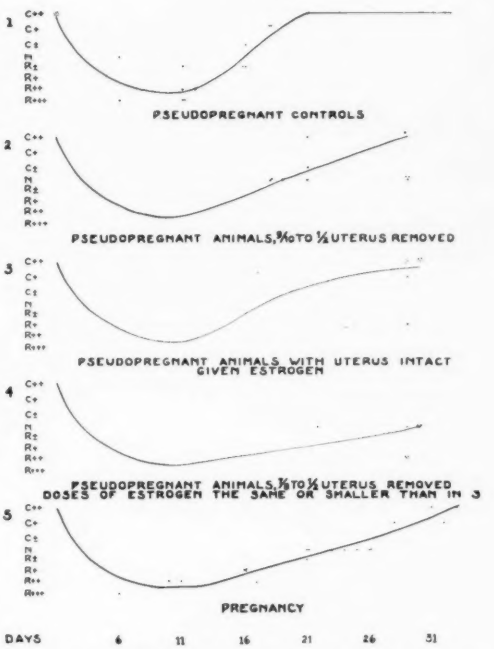


Fig. 2. The abscissas represent days following mating, or the induction of ovulation by injection of pregnancy urine. The ordinates indicate the type of response to pituitrin of the uterine muscle *in vitro*. $C++$, an extreme, estrus type contraction. $N$, No change in the spontaneous contractions. $R+++$, Relaxation of the muscle with inhibition of spontaneous contractions for 10 minutes or more. The intermediate points represent less extreme reactions.

trimmed close to the wall were weighed on a rough balance as soon as possible after removal. The percentage of uterus remaining was calculated from the weight of uterus removed at operation and that remaining at the end of the experiment. The weights and percentages are therefore only approximate. The reaction to pituitrin of the uterine muscle was tested by suspending a segment of uterus about 2 centimeters long in 125 cubic centimeters of Ringer's solution and recording the contraction on a kymograph. After spontaneous contractions had been established, first 0.5 unit and then 1 unit of pituitrin were added to the bath. The most extreme reaction obtained in each case has been recorded in the tables and plotted in Figure 2.

## EXPERIMENTAL OBSERVATIONS

*Group 1.* Pseudopregnant animals with varying amounts of the uterus removed were examined

TABLE IV.—PSEUDOPREGNANT ANIMALS WITH PART OF THE UTERUS REMOVED, GIVEN ESTROGEN

| Rabbit Number | Daily dose of estradiol benzoate—rat units | Day injections began | Day mated | Day examined | Ovulation | Reaction of uterus *in vitro* to pituitrin | Microscopic appearance of corpora lutea | Progestin effect in endometrium | Approximate amount of uterus remaining | | Number of corpora lutea | Weight of animal—grams |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | Proportion | Grams | | |
| Y 387 | 20 to 40 | 13 | Mating refused | 21 | — | N | — | Slight surface change | 1/2 | — | 11 | 4120 |
| | 80 | 21 | Mating refused | 29 | — | N | Generally well preserved | Slight perivascular change | 1/8 | — | | |
| Y 381 | 20 to 80 | 12 | — | 29 | — | R++ | Well preserved | Some progestational proliferation | 1/2 | 3.5 | 7 | 3620 |
| Y 399 | 20 to 80 | 11 | Mating refused | 29 | — | N | Beginning degeneration | Marked surface change | 1/4 | 3.2 | 9 | 4060 |
| Y 410 | 20 to 80 | 11 | 28 | 29 | No | C++ | Generally well preserved | Perivascular change | 1/4 | 1.9 | 5 | 3300 |
| Y 412 | 20 to 80 | 11 | 28 | 29 | No | R+++ | Generally well preserved | Surface change | 1/4 | 2.0 | 11 | 3120 |
| Y 419 | 20 to 80 | 11 | Mating refused | 30 | — | C+ | Ovaries lost | Perivascular change, necrosis | 1/4 | 2.7 | 6 | 3620 |
| Y 422 | 20 to 80 | 11 | Mating refused | 30 | — | R+ | Beginning degeneration | Slight perivascular change, some progestational proliferation | 1/4 | 3.0 | 12 | 3920 |
| Y 423 | 20 to 80 | 11 | 28 | 29 | No | R+ | Well preserved | Slight surface change | 1/4 | 1.8 | 12 | 3650 |

at various times after the 16th day (Table II). One totally hysterectomized animal, Y 345 (cervices remaining) showed well preserved corpora lutea in one ovary removed on the 26th day. At 50 days, the corpora in the remaining ovary were degenerate. Animals with nine-tenths to three-quarters of the uterus removed showed evidence of maintained function of the corpora lutea beyond 16 days as indicated by the reaction to pituitrin of the uterine muscle, and in some cases by the histological appearance of the corpora lutea, but not by any of the other criteria. There were well preserved corpora in Y 363 and Y 365 on the 18th day as well as slight evidence of continued progestational stimulation of the uteri, but this may be seen normally at this time, as shown by Y 342. The reaction to pituitrin of uterine muscles in these animals is shown graphically in Figure 2, *2*. Y 36 is of interest. At 21 days with nearly all the uterus remaining there were no signs of maintenance of the corpora. At that time one-half of the uterus, one horn, and one ovary were removed. Five days later the uterine muscle was refractory to pituitrin, and there was a fair progestational proliferation of the endometrium. The corpora lutea of the remaining ovary, although generally showing signs of degeneration, looked better preserved than would be expected from the appearance of the corpora in the ovary which had been removed at 21 days. This probably indicates a return of function of the corpora in the remaining ovary after partial hysterectomy. Removal of one ovary appears to have no such effect, as shown by Y 342, an animal with nearly all of the uterus remaining, in which one ovary was removed on the 18th day without any apparent effect 10 days later.

*Summary of group 1.* Removal of part of the uterus in the rabbit prolongs the life of the corpora lutea of pseudopregnancy and the degree of prolongation appears to be proportional to the amount of uterus removed.

*Group 2.* Pseudopregnant animals with the uterus intact and others with part of the uterus removed were given similar doses of estrogen. The results are shown in Tables III and IV. Estradiol benzoate, progynon B, was injected subcutaneously beginning on the 11th to the 13th day of pseudopregnancy. In most cases the doses were doubled after the 15th and 20th days. In some they were doubled only once and the same dose was given from the 16th day onward. Y 143 and Y 144, animals with intact uteri in which the amount of estrogen was adequate to maintain the corpora lutea, received 20 rat units from 11th to 15th days, 100 rat units from 16th to 20th days,

TABLE V.—PSEUDOPREGNANT ANIMALS GIVEN ESTROGEN WITH UTERUS INTACT AND THEN WITH PART OF UTERUS REMOVED

First pseudopregnancy—uterus intact

| Rabbit number | Daily dose of estradiol benzoate—rat units | Day injections begun | Day mated | Day uterus removed | Ovulation | Reaction of uterus *in vitro* to pituitrin | Progestin effect in endometrium |
|---|---|---|---|---|---|---|---|
| Y 415 | 20 to 80 | 11 | 28 | 29 | Yes | C++ | None |
| Y 424 | 30 | 11 | 28 | 30 | Yes | C+ | None |
| Y 425 | 30 | 13 | 28 | 29 | Yes | C++ | None |
| Y 426 | 30 | 13 | 28 | 29 | Yes | C++ | None |
| Y 427 | 30 | 11 | 28 | 29 | Yes | C++ | — |

Second pseudopregnancy—part of uterus removed

| Rabbit number | Approximate amount of uterus remaining | | Daily dose of estradiol benzoate—rat units | Day injections begun | Day examined | Day mated | Ovulation | Reaction of uterus *in vitro* to pituitrin | Progestin effect in endometrium | Microscopic appearance of corpora lutea | Number of corpora lutea | Weight of animal—grams |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Grams | Percent | | | | | | | | | | |
| Y 415 | 1.4 | 19 | 20 to 40 | 11 | 30 | 29 | No | N | Some progestational proliferation | Well preserved | 7 | 3860 |
| Y 424 | 1.6 | 18 | 30 | 11 | 30 | 29 | No | N | Surface change | Generally well preserved | 12 | 5060 |
| Y 425 | 2.3 | 27 | 30 | 13 | 29 | 28 | No | R++ | Surface change | Well preserved | 14 | 4860 |
| Y 426 | 4.1 | 35 | 30 | 13 | 30 | 29 | No | C++ | None | Generally well preserved | 14 | 3890 |
| Y 427 | 2.3 | 26 | 30 | 11 | 29 | Mating refused | — | R++ | Marked surface change | Well preserved | 10 | 3800 |

Controls—part of uterus removed, no estrogen

| Rabbit number | Approximate amount of uterus remaining | | Day mated | Day examined | Ovulation | Reaction of uterus to pituitrin | Progestin effect in endometrium | Microscopic appearance of corpora lutea | Number of corpora lutea | Weight of animal—grams |
|---|---|---|---|---|---|---|---|---|---|---|
| | Grams | Percent | | | | | | | | |
| Y 434 | 1.8 | 28 | Mating refused | 29 | — | C++ | None | Extreme degeneration | 8 | 3790 |
| Y 435 | 2.3 | 42 | 28 | 29 | Yes | C+ | None | Extreme degeneration | 9 | 3825 |
| Y 436 | 1.7 | 22 | 28 | 29 | Yes | N | None | Advanced degeneration | 8 | 3650 |
| Y 438 | 1.3 | 24 | 28 | 29 | Yes | N | None | Extreme degeneration | 9 | 3390 |

200 rat units from 21st to 25th days, and 400 rat units from 26th to 35th days. Most of the experiments were continued for 29 or 30 days. It will be noted that in the 7 animals with intact uteri given 20 to 80 rat units of estrogen a day, only 11 of 27 criteria indicated prolongation of the corpora lutea (Table III). In 8 animals with part of the uterus removed, on the other hand, 22 of 26 criteria indicated maintenance, none of the corpora showed more than beginning degeneration, and the endometria in all cases showed some evidence of the action of progesterone (Table IV). Even with twice this dose of estrogen, 40 to 160 rat units a day, 9 of the 19 criteria in 5 animals with the uterus intact indicated degeneration and the corpora lutea in 2 cases showed advanced degeneration (Table III). It is interesting that when the dose was larger, 40 to 160 rat units a day, perivascular changes were seen in the uterus. This is the result of larger amounts of estrogen

which were still insufficient to maintain the corpora lutea adequately, for as has been noted, perivascular changes are seen when there is an excess of estrogen in relation to progestin. The corpora lutea in these animals were degenerating, so that the amount of progesterone they were producing was smaller in relation to the estrogen than in the animals receiving less estrogen. The more normal proportion of estrogen and progesterone associated with maintenance of the corpora lutea is indicated by the surface change, since it appears in extreme degree in the sterile horn of unilaterally pregnant animals, in which perivascular changes and necrosis are not seen. Accordingly the surface change is seen only in cases in which most of the other criteria indicate maintenance of the corpora lutea, for in these the corpora lutea were adequately prolonged and there was no excess of estrogen.

*Summary of group 2.* Amounts of estrogen insufficient to prolong the life of the corpora lutea in animals with intact uteri, prolonged it in animals with part of the uterus removed as indicated by the majority of the criteria for determining the function of the corpora lutea.

*Group 3.* The thesis that partial hysterectomy spares estrogen, and its corollary that the amount of uterus determines how much estrogen will be necessary to maintain the corpora lutea, is most strikingly supported by this group of experiments. Five pseudopregnant rabbits with intact uteri were given doses of estrogen considered to be inadequate to maintain the corpora lutea. One received 20 to 80 rat units a day, the dose being doubled on the 16th and 21st day, and the rest received 30 rat units a day throughout (Table V). On the 28th day all of the animals mated. Subsequent examination revealed that ovulation had occurred in all cases and the gross appearance of the old corpora as well as the other criteria indicated that the corpora lutea were degenerate. Part of the uterus was removed at this time, and then during this second pseudopregnancy the animals were treated the same as they had been previously, except that one received a smaller amount of estrogen, and 2 were examined a day later, the 30th rather than the 29th. Four of the animals this time failed to ovulate (one would not mate) and, except for Y 426 in which the uterus was sensitive to pituitrin and the endometrium had returned to the condition of estrus, all of the criteria indicated maintenance of the corpora lutea in all of the animals. Y426 retained more of the uterus than any of the other animals: 4.1 grams, or 35 per cent, as calculated from the amount of uterus removed at the start of the experiment and that remaining at the end. Thus all of the criteria indicated degeneration when the uteri were intact, while with approximately 18 to 35 per cent of the uteri remaining, 17 of 19 of the criteria indicated maintenance. Rabbit Y415, in which the experiment in group 1 was run between the first and second parts of group 3, with only a little more uterus (some had to be removed for testing *in vitro*), showed no signs of maintenance of the corpora on the 22d day, 7 days earlier than the termination of the experiments in group 3. As further controls to these experiments, 4 pseudopregnant rabbits with comparable amounts of the uterus remaining, approximately 22 to 42 per cent, received no estrogen (Table V). These animals, also included in Table II, showed degeneration in 13 of 15 criteria on the 29th day. Those with the smallest amount of uterus remaining, approximately 22 and 24 per cent, showed failure of the uterus to contract to pituitrin. All of the other criteria indicated degeneration of the corpora lutea.

*Summary of group 3.* An amount of estrogen insufficient to prolong the life of the corpora lutea with the uterus intact, prolonged it in a second pseudopregnancy when part of the uterus had been removed. All of the criteria in 5 animals indicated degeneration of the corpora when the uteri were intact. With part of the uterus removed 17 of a total of 19 criteria indicated maintenance of the corpora lutea. The animal in which 2 of the criteria indicated degeneration of the corpora was the one retaining the most uterus. Four rabbits with comparable amounts of uterus removed, given no estrogen, showed degeneration of the corpora lutea in 13 of 15 criteria. The 2 animals in which one of the criteria indicated maintenance of the corpora were those retaining the smaller amounts of uterus.

### ANALYSIS OF THE CRITERIA

It is apparent from the data that no single criterion is reliable as an index of the function of the corpora lutea. The occurrence of ovulation after mating may be misleading, for animals will not always mate, and when they do ovulation may fail to occur even though there may be no corpora lutea (Y 418, Table I).

The reaction of the uterine muscle to pituitrin in the various experiments is represented graphically in Figure 2 in which it is compared with the reaction of the muscle in pseudopregnancy and pregnancy (sterile horn). It will be noted that in partially hysterectomized animals pseudopregnancy is prolonged, that is, the curve of reactivity of the muscle to pituitrin (Fig. 2, *2*) is more like

that of pregnancy (Fig. 2, 5) in which the corpora are naturally prolonged. In pseudopregnant animals with the uterus intact given an amount of estrogen which in general failed to prolong the life of the corpora, the curve (Fig. 2, 3) is little different from that of normal pseudopregnant animals (Fig. 2, 1). In pseudopregnant animals with part of the uterus removed given the same or smaller doses of estrogen the curve (Fig. 2, 4), is most like that of pregnancy, and many of the points indicate maintenance of function of the corpora even beyond that occurring in pregnancy. The *in vitro* reaction of the uterine muscle appears to be the most sensitive criterion of the corpus luteum function, for the small amount of progestin produced by the histologically degenerate corpora lutea of Y 418, Y 436, and Y 438 (Table II), insufficient to prevent ovulation, was still enough to render the uteri of these animals refractory to pituitrin.

The microscopic appearance of the endometrium is of particular interest because, although it may indicate a state of estrus when other criteria indicate action of progesterone and hence alone is not a reliable criterion, it often indicates the relative proportion of estrogen and progesterone. When the corpora are adequately maintained and there is an excess of estrogen, perivascular changes and necrosis occur, for example, Y143 (Table III). These changes are also seen when the corpora lutea have been allowed to degenerate by the giving of too little estrogen and hence are again producing too little progesterone to balance the estrogen. The surface change is seen when most of the other criteria indicate optimal estrogen dosage for maintenance of the corpora. Progestational proliferation 29 days after ovulation probably indicates insufficient dosage of estrogen, allowing the endometrium by insufficient stimulation of the corpora to regress to the condition of estrus and then, due possibly to the increasing dosage of estrogen, since it is seen only in animals in which the dose was increased, bringing about a late increase in production of progesterone. This theory is borne out by the findings in Y 36 (Table II) already discussed. Progestational proliferation cannot be maintained beyond 16 days; it must be transformed into a late pregnancy type of endometrium (surface change) or it will regress to a condition of estrus (4). That slight perivascular changes are seen along with it in Y 422 (Table IV) is consistent with this. It indicates insufficient estrogen to maintain the corpora lutea adequately at an earlier time, allowing the original progestational proliferation to regress and causing slight perivascular changes. Then the increasing dose of estrogen revived the corpora, and progestational proliferation began again.

The microscopic appearance of the corpora lutea is a good criterion, for although corpora which appear degenerate may still be producing a little progestin as indicated by other criteria, well preserved corpora always prove to be functional, and in general the more degenerate the corpora appear the less evidence of function there is as indicated by the other criteria.

The number of corpora lutea seems to have nothing to do with whether or not they are maintained by estrogen. For example there was no evidence of maintenance in either Y 413 with only 5 corpora lutea or Y376 with 10 (Table III). When the life of the corpora has been prolonged, however, the evidence of corpus luteum function is more complete when there are large numbers of corpora lutea. Thus in Table IV, in animals in which there are 11 and 12 corpora the evidence of maintenance is fairly complete, while in those with 5 or 6 there is evidence of degeneration in one or more criteria. Y410 and Y 419 (Table IV) with 5 and 6 corpora lutea, respectively, were the only animals with part of the uterus removed to show contraction of the uterine muscle to pituitrin *in vitro*. They also showed the perivascular change and necrosis in the endometrium, signs of the action of both estrogen and progesterone with an excess of estrogen. It is probable that when there were more corpora, more progesterone was produced. This is reasonable, for a quantitative relation between the number of corpora lutea and the degree of progestational proliferation in the rabbit has been shown (8, 16).

## RELIEF OF MENOPAUSAL SYMPTOMS FOLLOWING SUBTOTAL HYSTERECTOMY

The question of whether hysterestomy in the human being has any effect on the endocrine system is an important one and, although there are numerous opinions, the evidence does not lead to an answer. The subject was reviewed by Reynolds in 1939 (31). The following case is of interest because it may represent the sparing of estrogen following hysterectomy in the woman.

M.S., a 44 year old woman, tripara, who had experienced symptoms of hypoestrinism for more than a year and a half, needed a subtotal hysterectomy because of the presence in the uterus of fibromyoma causing pain and menorrhagia. The menopausal symptoms consisted of hot flashes, recurrent dizziness, and nervousness. During the year before operation, her symptoms had been relieved by the injection of estrogens. A dilatation and curettage, done before treatment with estrogen was begun, revealed normal endometrium. General physical examination was negative; blood count was normal; blood pressure was

140/80. There was no evidence of atrophy of the vaginal mucosa and the vaginal smear was normal. A 135 gram uterus containing a 4 by 5 by 5 centimeter fibromyoma was removed on the 3d day of a menstrual period. Both tubes and ovaries and the cervix were left. Both ovaries were normal in size and appearance. One of them contained what appeared to be a slightly shrunken corpus luteum. Section of the uterus showed a menstruating endometrium. Areas of the endometrium which were intact were thin and only scattered glands showed any evidence of secretion, suggesting that there had been little corpus luteum effect. For 3½ months following operation the patient was entirely free of dizziness and nervousness, previously her most distressing symptoms, and she had only an occasional mild hot flash. Since the recurrence of her symptoms she has again been relieved by the injection of estrogens. Nervousness, manifested particularly by a crowding sensation in the epigastrium, has just begun to recur 12 months after operation. A possible explanation of these observations is that the removal of the uterus spared the decreasing supply of estrogen to such an extent that the level at which symptoms of hypoestrinism occurred was not again reached for 3½ months. It is possible also, that the corpus luteum noted at operation was maintained or revived for a time, for there is evidence that the life of the corpus luteum in the woman may be prolonged by estrogenic hormone (38). The findings in this case are not proof of an endocrine effect of hysterectomy, for subjective symptoms of the type experienced in this case might be relieved by any operation, although the dilatation and curettage a year before had no such effect. The appearance of the vaginal mucosa and of the vaginal smear were not available as criteria of estrogen action, since they were normal to start with. Assays of the excretion of estrogen, gonadotropic hormone, and pregnandiol, had they been done in this case, might have supplied needed objective evidence.

It seems reasonable to conclude from the experiments presented that the prolongation of the life of the corpora lutea in the rabbit following hysterectomy is caused by the sparing of estrogenic hormone produced in the organism, probably by growing follicles in the ovaries. The work of Westman (37) and of Westman and Jacobsohn (41) has shown the importance of the production of estrogen by the graafian follicles for the normal development and maintenance of the corpus luteum in the rabbit.

It has been reported that hysterectomy is without effect on the ovarian cycle in the monkey (5), opposum (12), and rat (25, 28). In the case of the monkey and the opposum, the experiments do not prove that some prolongation of the life of the corpus luteum does not occur after hysterectomy, but it appears that there is no prolongation comparable to that in the rabbit and guinea pig. In the rat the corpus luteum of pseudopregnancy, that is, following mating or mechanical stimulation of the cervix, is maintained by hysterectomy, while that forming spontaneously, in the absence of mating, normally lasting only about 4 days as compared with 8 to 12 in pseudopregnancy, is unaffected (3, 13). It is reasonable to suppose that hypophyseal activity is responsible for the different behavior of the corpora lutea after mating or mechanical excitation of the cervix, since such a stimulus might produce greater or more prolonged secretion of gonadotropic hormone by the pituitary. The effect on the corpora lutea might be mediated through the ovarian cortex by the stimulation there of the production of estrogen. It is known that the corpora lutea of the rabbit can be maintained by the injection of estrogen in the absence of the hypophysis (33, 40), and that estrogen is essential for their normal development and maintenance (37, 41). It may be that in the rat, without increased production of estrogen stimulated in the ovary by the hypophyseal secretion resulting from copulation, there is insufficient estrogen, even after it is spared by hysterectomy, to prolong the life of the corpora lutea beyond 4 days.

Evidence of the metabolism of the estrogens by the uterus has been brought forward (29). Whether the endometrium or the uterine muscle is more important in the utilization of estrogen or conversion of estrogen to less active compounds is a question which, if answered, might help to explain the maintenance of the corpora lutea in the rat incident to uterine distention by wax pellets following pregnancy (34). The factor of estrogen sparing might be of importance if it were found that the endometrium is the greater user of estrogen, for with distention of the uterus by wax pellets there would be some reduction of the endometrial mass by pressure, although the amount of muscle would be increased due to hypertrophy (32). Such a mechanism is suggested by an experiment not included in the foregoing data. Rabbit Y 393 with one horn of the uterus removed received 20 to 80 rat units of estrogen, an amount usually insufficient to maintain the corpora in intact animals. On the 29th day, examination revealed that the remaining uterine horn was greatly distended with pus (pyometrium), with resulting hypertrophy of the wall and complete destruction of the endometrium. The remaining uterine muscle weighed 25 grams, as much or more than the normal intact uterus, yet the corpora lutea were generally well preserved microscopically, perivascular changes were noted in the myometrium and the reaction of the muscle to pituitrin was C + −, indicating some activity of the corpora. Y 376 (Table III) with the same total weight of uterus received the same dose of estrogen, but showed no evidence of maintenance of the corpora whatever. This suggests that in the animal with the pyometrium, even though there was more uterine muscle than normally, sufficient estrogen was spared by the

absence of the endometrium to prolong the life of the corpora lutea.

Whether the greater need for estrogen lies in the endometrium or the myometrium, it is clear that the size of the normal uterus determines the amount used. From this it is interesting to speculate on the possible significance of the underdeveloped, infantile uterus in women. It is conceivable that the production of estrogen by the ovaries might be such that, with the sparing effect of the undersized uterus, hyperestrinism of varying degree might result. If estrogen inhibits the gonadotropic activity of the hypophysis in the woman as it does in experimental animals (10, 27), it is possible that a relative excess of estrogen resulting from an undersized uterus might prevent normal establishment of the menstrual cycle. It is also possible that in some cases the excess of estrogen which produces hyperplasia of the endometrium might arise in this way. This condition may be produced experimentally in women as well as in experimental animals by the injection of estrogenic hormone in large amounts, and increased excretion of estrogen in the urine has been reported in association with it (42). It is accompanied by the persistence of a follicle in the ovary (failure of ovulation and corpus luteum formation). The idea that the pituitary is responsible for failure of proper development and rupture of the follicle is not new (43). The pituitary failure may not always be the primary cause, however. Like the hyperplasia of the endometrium, it might result from hyperestrinism, and the uterus, perhaps the endometrium itself, might cause the disturbance by not using up its share of estrogenic hormone. In a recent report of the production by estradiol benzoate of hyperplasia in castrated monkeys Cleveland, Phelps and Burch (7) noted that only in animals in which the amount of the uterus had been decreased by previous biopsies, was hyperplasia obtained. It seems in these experiments that the size of the uterus (the amount remaining) determined whether or not a given amount of estrogen would have a pathological effect on the endometrium. In the animals from which biopsy specimens had been removed from the uterus, the effective amount of estrogen was greater because there was less uterus to use it up.

If the underdeveloped uterus stops the normal endocrine balance by sparing estrogen which in turn inhibits the gonadotropic activity of the pituitary, enlargement of the uterus might be expected to remedy the situation by decreasing the estrogen level and allowing the hypophysis to stimulate the ovaries to more normal function. The ovarian enlargement observed following the use of uterine stems (6, 9, 36), which by distention of the uterine cavity caused hypertrophy of the uterus, may be an evidence of this mechanism. Not only uterine and ovarian enlargement have been reported following the use of intrauterine stems, but the relief of amenorrhea, dysmenorrhea, and even sterility as well. It is possible that the uterus of inadequate size acts as a block to normal hormonic relations between the hypophysis and the ovaries by not using its share of estrogen. The evidence suggests that a quantitative balance may be essential between the production and utilization of estrogenic hormone for the normal function of the sexual organs in the female.

## SUMMARY

The life of the corpora lutea of pseudopregnancy in the rabbit may be prolonged by removal of part of the uterus. The degree of prolongation appears to be proportional to the amount of uterus removed.

An amount of estrogen insufficient to prolong the life of the corpora lutea of pseudopregnancy in rabbits with intact uteri may maintain the corpora lutea beyond the usual time when it is given to rabbits with a part of the uterus removed.

An amount of estrogen insufficient to prolong the life of the corpora lutea in rabbits with intact uteri may prolong it in a second pseudopregnancy after part of the uterus has been removed.

The amount of estrogen necessary to prolong the life of the corpora lutea in partially hysterectomized rabbits is determined primarily by the amount of uterus remaining.

A case is presented in which menopausal symptoms in a 44 year old woman were relieved following subtotal hysterectomy, suggesting an estrogen sparing effect in the human being.

The possible relation of sparing of estrogen to the maintenance of the corpora lutea in the rat after hysterectomy and following distention of the uterus by wax pellets is discussed.

It is suggested that in women with underdeveloped uteri a condition of relative hyperestrinism may result from the sparing of estrogenic hormone, causing a block in the pituitary-ovary relationship by suppression of the gonadotropic activity of the hypophysis.

## CONCLUSIONS

Estrogenic hormone is spared by removal of the uterus. The prolongation of the life of the corpora lutea by hysterectomy in the rabbit is a manifestation of the sparing of estrogen produced in the organism.

## REFERENCES


1. Allen, W. M., and Heckel, G. P. Science, 1936, 84: 161.
2. Asdell, S. A., and Hammond, J. Am. J. Physiol., 1933, 103: 600.
3. Bradbury, J. T. Anat. Rec., 1937, 70: 51.
4. Allen, W. M. Cold Spring Harbor Symp. Quant. Biol., 1937, 5: 66.
5. Burford, T. H., and Diddle, A. W. Surg. Gyn. Obst., 1936, 62: 701.
6. Carstens, J. A. Am. J. Obst., 1903, 48: 720.
7. Cleveland, R., Phelps, D. and Burch, J. C. Endocrinology, 1941, 28: 659.
8. Corner, G. W. Am. J. Physiol., 1928, 86: 74.
9. Dickinson, R. L., and Smith, W. S. Am. J. Obst., 1913, 68: 686.
10. Haberlandt, L. Arch. ges. Physiol., 1927, 216: 525.
11. Hammond, J. Reproduction in the Rabbit. Edinburgh, London: Oliver and Boyd, 1925.
12. Hartman, C. G. Am. J. Anat., 1925, 35: 25.
13. Hechter, O., Fraenkel, M., Lev, M. and Soskin, S. Endocrinology, 1940, 26: 680.
14. Heckel, G. P., and Allen, W. M. Am. J. Physiol., 1936, 116: 73.
15. Idem. Endocrinology, 1939, 24: 137.
16. Joublot, J. Arch. anat., Strasb. 1927, 7: 435.
17. Knaus, H. Arch. Gyn., 1929, 138: 201.
18. Ibid, 1930, 140: 191.
19. Ibid, 1930, 141: 374.
20. Ibid, 1930, 141: 395.
21. Loeb, L. Arch. Entwmech., 1909, 27: 89.
22. Loeb, L. Proc. Soc. Exp. Biol., N. Y., 1923, 20: 441.
23. Loeb, L. Am. J. Physiol., 1927, 83: 202.
24. Loeb, L., and Smith, M.G. Am. J. Anat., 1936, 58:1.
25. Long, J. A., and Evans, H. M. Mem. Univ. California, 1922, 6.
26. Makepeace, A. W. Am. J. Obst., 1939, 37: 457.
27. Meyer, R. K., Leonard, S. L., Hisaw, F. L., and Martin, S. J. Proc. Soc. Exp. Biol., N.Y., 1930, 27: 702.
28. Murphy, D. P., Anat. Rec., 1934, 60: 77.
29. Pincus, G. Cold Spring Harbor Symp. Quant. Biol., 1937, 5: 44.
30. Pincus, G., and Kirsch, R. E. Am. J. Physiol., 1936, 115: 219.
31. Reynolds, S. R. M. Physiology of the Uterus. New York and London: P. B. Hoeber, 1939.
32. Reynolds, S. R. M., and Kaminester, S. Am. J. Physiol., 1936, 116: 510.
33. Robson, J. M., J. Physiol., 1937, 90: 435.
34. Selye, H. Proc. Soc. Exp. Biol., N.Y., 1934, 31: 488.
35. Sessums, J. V., and Murphy, O. P. Surg. Gyn. Obst., 1933, 56: 600.
36. Weir, W. H. Am. J. Obst., 1937, 33: 291.
37. Westman, A. Arch. Gyn., 1934, 158: 476.
38. Westman, A. Endocrinology, 1940, 26: 774.
39. Westman, A., and Jacobsohn, D. Acta obst. gyn. scand., 1937, 17: 1.
40. Ibid, 1937, 17: 13.
41. Ibid, 1937, 17: 476.
42. Zondek, B. Zbl. Gyn., 1930, 1: 1.
43. Idem. Genital Functions and their Hormonal Regulation. P. 217. Baltimore: Williams & Wilkins Co., 1941.

# EDITORIALS

SURGERY
Gynecology and Obstetrics

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1905–1935

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SEPTEMBER, 1942

## PRACTICAL CONSIDERATIONS OF OVARIAN TUMORS

THE range of variety exhibited by the diverse types of ovarian neoplasms makes for difficulty in the surgical handling of these lesions. For the surgeon who has facilities for immediate diagnosis by means of the fresh-frozen section technique, this difficulty is obviated, more or less, but where such facilities are not available gross identification becomes a matter of paramount importance. The following observations may serve as useful generalizations in determination of the type of surgical treatment to be employed in individual cases.

Eighty per cent of ovarian tumors are cystic, and the majority of these are benign. Twenty per cent are solid, and approximately two-thirds of these are malignant.

Simple cysts usually are small and frequently are bilateral; are smooth of surface and never contain papillary excrescences. The lutein type of cyst will reveal a thin yellowish line on inner surface of its capsule.

Endometriomas are perforating cysts and adhere to neighboring structures. They possess a tarry content and are accompanied by punctate bluish-black nodules on the pelvic peritoneum. Conservative treatment may sometimes be employed provided complete destruction of ovarian tissue has not occurred.

Eighty per cent of cystadenomas appear as unilateral, unilocular, or multilocular cysts with thin semitransparent walls. Usually larger than simple cysts, they possess, like the aforementioned, smooth capsules free from superficial excrescences. Whenever possible, however, they should be removed intact to obviate two dangers: namely, soiling of the peritoneum by mucoid contents (60 per cent) and peritoneal seeding from "concealed" intracystic papillary carcinoma.

Fibrous papillary cystadenoma (intracystic and extracystic papillary fibroma) may occur as a unilateral or a bilateral ovarian cyst, or it may be primary in the parovarium. Usually unilocular, it possesses intracystic or extracystic hard, white, warty excrescences. Although papillary carcinoma sometimes is associated with this lesion, the combination is unusual and can be detected by a softer consistency and more luxuriant villous growth of malignant portion. In the benign papillary form peritoneal "implants" are not observed.

Dermoids may be readily recognized by their somewhat yellowish color and their opacity. Here again the surgeon should avoid rupture whenever possible, because the oily contents are highly irritative, eliciting a "granulomatous" type of peritoneal reaction. Malignancy in a dermoid can be detected upon the opening of the cyst. Dermoids are bilateral in 10 to 15 per cent of cases and in-

nocent-appearing cysts on the contralateral ovary should be diagnostically aspirated. It is sometimes possible to shell out a small dermoid and thus preserve a remnant of functioning ovarian tissue.

A papillary cystadenocarcinoma is characterized by intracystic and extracystic delicate, frond-like excrescences. Bilateral in 35 per cent of cases, particularly in its extracystic form, the lesion is associated with peritoneal implants and with ascites. However, in the absence of massive metastatic "caking" of the omentum "almost-miracles" can be wrought by removal of the primary neoplasm, with hysterectomy. This happy result occurs after removal of lesions principally of grade 1 (Broders), but occasionally of higher grade and postoperative roentgen therapy is used.

In the more undifferentiated forms of cystadenocarcinoma, simple papillary excrescences are replaced by solid nodules of tumor tissue. These nodules may appear on the inside of an intact capsule or may present themselves in the form of superficial bosselations. Bilaterality is a feature in about 40 per cent and solid "caking" of the omentum raises the important question of operability. In such cases metastasis will be found in the uterine cavity very frequently. This type forms the connecting link between cystic and solid carcinomas.

Ovarian fibroma is a solid or solid-cystic neoplasm unilateral in most of the observed instances. The shiny smooth surface, pure white color and extreme density on section are diagnostic features. Ascites frequently and hydrothorax occasionally are noted when large specimens are present. Failure to keep this fact in mind may result in denying patients the benefit of surgical exploration for a tumor that is practically always benign.

Primary solid ovarian carcinoma is bilateral in 50 per cent of cases and frequently is inoperable because of local extension or distant metastasis. Removal is often possible when the lesion is encapsulated, but even in this circumstance recurrence is common. Necrosis, hemorrhage, local adhesions and nodular superficial projections are unfavorable features, especially in large, soft tumors of this type. The grade of the lesion is usually high, the primary operative mortality rate is considerable and the five year survival rate is less than 30 per cent. When unilateral, firm encapsulated lesions of lower grade are present, prognosis is, in general, good.

If the patient is an adolescent, if the tumor is unilateral, encapsulated, and of brainlike consistency, it probably is a dysgerminoma. An infantile uterus is confirmatory evidence of this. Because this tumor does not tend to spread rapidly and as it is very radiosensitive, surprisingly good results can be had even after local removal of the lesion. It represents the paradox of a grade 4 malignant neoplasm which is accompanied by a good prognosis.

Granulosa cell tumor often can be diagnosed on the basis of the clinical history. Sixty per cent occur among women who have passed the menopause, and recurrent periodic "menstruation-like" bleeding is characteristic. The tumor is unilateral, solid and encapsulated, with a cut surface which has the color and consistency of liver sausage. The uterus usually is two to four times normal size. Prognosis is good. Although conservative surgery may not be so important among older women who have this tumor, the importance of preservation of the contralateral ovary becomes paramount in the young, for if it is not removed, pregnancy becomes possible.

Theca cell tumor is associated with a clinical history similar to that of tumors of the granulosa cell group. The neoplasm is solid and resembles fibroma. A yellow color on the surface and on section makes possible a gross diagnosis. It usually is benign.

Finally, mention should be made of metastatic tumors. If the lesion is bilateral, solid and encapsulated; if it is nodular on the surface and maintains the general contour of the ovary; if the cut section is of "rubbery" consistency and "retracts," then search should be made for a primary lesion in the gastrointestinal tract. When these metastatic lesions are present twisting of the ovarian pedicle may occur and the tumors therefore should be removed. Hysterectomy, however, is in this particular instance a useless procedure, because the ultimate outlook is, unfortunately, hopeless.

Sir Benjamin Brodie has wisely said, "When we know not what to do it is best that we do nothing." Perhaps, however, "what to do" about ovarian tumors may become more apparent through judicious evaluation of these simple rules of diagnosis.

MALCOLM B. DOCKERTY.

## PHYSIOPATHOLOGICAL SIMILARITIES OF SHOCK SYNDROME IN PREPERFORATIVE APPENDICITIS AND CUTANEOUS BURN

THE peritoneum is approximately one-one-hundredth the thickness of the skin and is sparsely supplied with blood vessels, nerves and lymphatics, while the skin is abundantly supplied. The total surface of the parietal and visceral peritoneum and that of the skin are approximately the same. Both are composed of epithelial and connective tissue cells; in both, healing follows partial devitalization by replacement of these cells; both the peritoneum and skin protect vital inner structures; both act as barriers to bacterial invasion; both are normally moist to prevent or reduce surface friction; and, both absorb and secrete.

Subclinical peritoneal shock is so designated because, preceding clinical manifestations, evidence of the shock syndrome is to be found by chemical analysis of the blood. Hemoconcentration and diminished plasma and blood volume precede and accompany these clinical manifestations. Occasional cases of preperforative appendicitis produce this type of shock. Clinical peritoneal shock is present during the terminal phases of a spreading peritonitis. It may be masked by the symptoms and signs accompanying the pathological changes which are frequently sudden in onset, as in the case of acute perforation of a duodenal ulcer or an acute pancreatitis.

Erythema, widening and prolongation of capillary and lymph vessels, extravasation of plasma into cavities and tissue spaces with associated hemoconcentration, and hypoproteinemia, followed by diminished red cell volume, occur in patients with preperforative appendicitis and cutaneous burns of moderate degree. In the peritoneum, the gross changes are not as evident as in the skin where the injury induced by the heat causes dilation of the capillaries with increased exudation of plasma through the capillary walls. The cause of the dilatation of the capillaries in the peritoneum is the action of bacterial toxins but the end-result, increased capillary permeability, is identical. The loss of plasma accompanying burns is external and interstitial. In preperforative appendicitis, the fluid leaks into the peritoneal cavity, into the preperitoneal, parietal, and visceral peritoneal tissue spaces and into the deeper coats of the intestine or stomach adjacent to the lesion.

The extravasation of plasma in burns occurs immediately and attains its maximum in point of time and amount in from 36 to 40 hours; in preperforative appendicitis in man and in the preperforative induced gangrenous appendix in the dog, we have collected plasma in

amounts sufficient to be analyzed for proteins within a period of 2 hours. The amount of plasma loss in burns varies with the extent and severity of the lesion.

In 1930, Underhill, Kapsinow, and Fisk estimated from experiments on rabbits that a man weighing 65 kilograms who has sustained a superficial burn involving one-sixth of his body surface will have lost 70 per cent of his plasma within the first 24 to 36 hours, a total of 3,500 cubic centimeters; if one-third of the body surface were involved, 7,000 cubic centimeters, the limit to which the organism may give up its reserve water if it is to maintain blood volume constant. Estimations of the amount of plasma which leaks from the blood vessels into the peritoneal cavity and tissue spaces are not so definite. In one patient with preperforative gangrenous appendicitis — male, weight 50 kilograms—400 cubic centimeters of plasma were estimated to have been present in the peritoneal cavity. No attempt was made to judge the apparently large amount of fluid lost in the perperitoneal, parietal, and visceral peritoneal tissue spaces.

Chemical examinations of the fluid which extravasates from the blood following burns and into the peritoneal cavity in preperforative appendicitis show that the proteins and electrolytes are approximately the same. In 1930, McIver analyzed blister fluid and found total proteins to be 3.7 per 100 cubic centimeters and chlorides 591. We have just reported that the protein content of the peritoneal exudate in preperforative appendicitis is approximately the same as blood plasma and that apparently a relationship exists between the type of the pathological lesion and the albumin-globulin content of the blood plasma. We have also demonstrated that the plasma chloride level in preperforative appendicitis is adequately maintained. In 1930, Underhill observed that in burns as much as 36 per cent of the sodium chloride of the blood may be lost without causing alteration in the chloride content of the blood.

In both superficial cutaneous burns and in the peritoneal changes secondary to preperforative appendicitis in man and induced gangrenous appendix in dogs, reabsorption of plasma occurs. Underhill has shown that while in the early stages of a burn the cell changes in the capillary permit the extravasation of plasma, reabsorption into the capillary does not occur until approximately the fortieth hour. Our observation in dogs show that as the localizing process (an early appendiceal perforation walled off by a fibrous exudate, adherent loops of intestine, or omentum) progresses toward the stage of abscess formation, the amount of peritoneal exudate diminishes. This occurs usually 48 hours after ligation of the appendix. It will be of importance to determine what effect this reabsorption has on total circulatory protein content of blood.

Thus, while there are some anatomical structural differences in the peritoneum and skin, numerous close similarities may be noted. Subclinical shock (hemoconcentration, fall in plasma and blood volume, decrease in amount of circulating protein) occurs in both preperforative appendicitis in man and induced gangrene of the appendix in dogs and in superficial burns in man. Increased permeability of capillaries occurs in both preperforative appendicitis and in cutaneous burns in both man and the dog. The time of appearance of plasma in the interstitial spaces and in the peritoneal cavity; the amount of plasma loss; the protein and electrolytic content; and the phenomenon of reabsorption of plasma in shock due to reaction of the peritoneum to preperforative appendicitis in man and induced gangrene in the dog and to superficial cutaneous burns in man, are all similar.

JOHN O. BOWER.
J. G. REINHOLD.

# THE SURGEON'S LIBRARY

## REVIEWS OF NEW BOOKS

A BRIEF book, *Subacute Bacterial Endocarditis*,[1] is presented by Emanuel Libman and Charles R. Friedberg, and edited by Henry A. Christian.

In the foreword Henry A. Christian states that recent advances in chemotherapy have made possible a new therapy of many infectious diseases, but for many of them the results remain far from satisfactory. He commends this volume to the reading medical public because of the need for early diagnosis of subacute bacterial endocarditis, if more effective therapy is to be possible.

The authors, eminent authorities with life long interest in the disease, have drawn from the wealth of their personal experience and the world literature to present a complete, well balanced study of a difficult subject.

In the classification of bacterial endocarditis they prefer the term subacute even in cases lasting a year or more, because these prolonged cases are not really chronic in the sense of glomerulonephritis, tuberculosis, or valvular heart disease. They recognize it as a common disease and one of them (E.L.) observed personally 1000 cases from 1899 to 1930.

In a brief but concise discussion of etiology they state that in over 90 per cent of the cases the causative organisms are nonhemolytic streptococci, usually of the alpha (viridans) variety. As a rule it is the patients with valvular defects, who have few or no symptoms, who are most subject to the disease. The symptoms of the disease are thoroughly discussed and special attention given to those which appear after "grippal" infections, operative procedure, pregnancy and puerperium, but it is often not possible to say whether these associations are merely coincidental or causative.

Eleven pages with 7 excellent illustrations are given to the essential discussion of pathology. The fact is stressed that the fundamental feature of the disease is the presence of bacterial vegetations on the heart valves which contain bacteria and are readily washed off into the blood stream giving rise to the bacteriemia, toxemia, and the occurrence of embolic phenomena.

The symptom complex arises from the endocardial involvement or its complications. The early combination of symptoms is such as to simulate a variety of diseases with resulting confusion and the authors have given close attention to the general signs and symptoms with special reference to the involvement of individual organs.

The recognition of mild cases and the differentiation between the "bacteria free stage" and "recovery" are emphasized. These terms are arbitrary and were introduced by one of the authors (E.L.) some years ago. Their concept is completely expressed in 18 pages with 7 illustrations.

In the general discussion of prognosis, the authors state that they have personally observed at least 25 cases of spontaneous recovery. Twelve of these are reported in detail and are called recovered cases. They recommend that prophylaxis be directed particularly to cases in which there is a valve lesion causing no, or but trifling, discomfort. All infection should be avoided, eliminated if present, and one of the new chemotherapeutic agents should be administered before and after surgical procedure.

The authors discuss all of the acceptable forms of treatment and conclude that while therapy remains unsatisfactory chemotherapy, particularly the use of sulfapyridine, seems to offer the greatest promise of cure. The importance of general supportative measures, early blood transfusion, and the need for a more effective chemotherapeutic agent are emphasized. This volume is easy to read, interesting, and complete. It is a valuable asset in any medical library but especially to the student of medicine and the busy practitioner. GEORGE C. TURNBULL.

THE volume of 897 pages by Dr. Kugelmass on *Blood Disorders in Children*[1] indicates somewhat the vast amount of material that has accumulated in this field. The book was written for practitioners and pediatricians to help solve blood problems seen in everyday practice in sick children. The order of the various sections of the book are as follows: (1) the hemopoietic system embracing the blood and blood forming organs in health and disease; (2) the erythron embodying the normal red cell mechanism; the anemias, polycythemias and pigment disorders; (3) the leucon comprising the normal white cell mechanism, the myeloid, lymphoid, and monocytic disorders, and the leucemias; (4) the thrombin covering the normal clotting mechanism and the essential and vascular hemorrhagic disorders; (5) the reticuloendothelial system including the normal mechanism and congenital lipidoses; (6) finally, the blood picture characteristic of systemic and infectious diseases.

[1] SUBACUTE BACTERIAL ENDOCARDITIS. By Emanuel Libman, M.D., and Charles K. Friedberg. Edited by Henry A. Christian, A.M., M.D., LL.D., Sc.D.(Hon.), F.A.C.P., Hon. F.R.C.P.(Can.). (Reprinted from Oxford Loose-Leaf Medicine). London, New York, and Toronto: Oxford University Press, 1941.

[1] BLOOD DISORDERS IN CHILDREN. By I. Newton Kugelmass, M.D., Ph.D., Sc.D.Spéc. London, New York, and Toronto: Oxford University Press, 1941.

The brief historical outlines preceding each chapter are interesting and useful. At the end of the book are a blood glossary and an outline of symptom diagnosis.

The book is published on glossy paper and the format makes for easy reading. The book is written in an extremely general manner. There are few specific references to the source of material in the body of the text. A few key references are added at the end of each chapter. Because of frequent repetition in certain sections, the size of the book could probably be reduced considerably. Numerous statements presented factually are still controversial in the field of hematology, e.g. the presence of a splenic hormone, the relation of so-called vitamin P to vascular purpura in man, the use of a diet for increasing the clotting time of the blood, etc.

The illustration of blood cells on page 9 is the same as that in Whitby and Britton's *Disorders of the Blood* but no acknowledgment of the source is given.

The classification of the anemias under the headings, "deficiency," "dyspoietic," "hemolytic and hemorrhagic," is simple and practical. The sections on hemolytic anemia and hemorrhagic diseases are especially comprehensive. Representative case histories illustrate many aspects of the various blood disorders.

It is a question whether there is a definite need for a book of this type. Most of the information needed by the practitioner can be obtained from a good general text on hematology. The pediatrician will probably find the volume useful as a reference source.

HAROLD L. ALT.

# CORRESPONDENCE

## THE GENERAL SURGEON'S APPROACH TO THE PROBLEMS PRESENTED BY FRACTURES AND OTHER TRAUMA

*To the Editor:* The following letter was recently received by me:

From the office of Surgeon Rear-Admiral Cecil P. G. Wakeley
Royal Naval Hospital
Haslar, Gosport
Hants.
26th May, 1942

"Dear Professor Lee,

"I have read with great interest your article on 'The General Surgeon's approach to the problems presented by Fractures and other Traumas,' which was published in *Surgery, Gynecology and Obstetrics* in February of this year.

"Your Figure 1 showing 'Wound of face resulting from high explosive bombs' was a case of mine and I notice that you put 'By courtesy of Mr. Broster.'

"When Mr. Broster went to America last year he asked me for some pictures of wounds as he was giving a paper in America. This paper has since been published in the *Annals of Surgery* where due credit was given to me for my pictures; now I see that Mr. Broster is credited with them.

"As these pictures are likely to be published further here later I should like to point out that the copyright is mine and not Broster's.

"I hope you will excuse me pointing out this to you but it is simply to prevent controversy at a later date.

"With all good wishes,

"Yours sincerely,

(Signed) CECIL P. G. WAKELEY"

I am sorry that I had forgotten that this photograph had been borrowed by Mr. Broster from Mr. Wakeley. Credit for the illustration should be given Mr. Wakeley.

WALTER ESTELL LEE

Philadelphia,
Pennsylvania.

# CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

W. EDWARD GALLIE, Toronto, *President*
IRVIN ABELL, Louisville, *President-Elect*

*Committee on Arrangements*
THOMAS E. JONES, *Chairman;* JOHN W. HOLLOWAY, *Secretary*

## 1942 CLINICAL CONGRESS IN CLEVELAND—A WAR SESSION

AS the Stevens Hotel in Chicago has been taken over by the Army for its Air Corps Training School, it was necessary to make a change in the plans for the 1942 Clinical Congress. The date and place of the 1942 session have been changed to November 17–20, in Cleveland, with headquarters at the Cleveland Public Auditorium, which provides exceptional facilities, so that all activities of the Congress, excepting the clinical program, will be located in that building.

Under the direction of the Board of Regents a four-day program is being developed for the thirty-second annual Clinical Congress, which will be based upon the many medical and surgical problems that arise out of the prosecution of an all-out effort to win the war, emphasizing the needs of the rapidly expanding medical services of the Army and Navy and consideration of the special problems related to the increasing activities for civilian defense. These subjects will highlight the programs for the scientific sessions at headquarters and will provide the basis for many clinical demonstrations at the hospitals.

### CLINICAL PROGRAM

The surgeons of Cleveland have organized with Dr. Thomas E. Jones as chairman and Dr. John W. Holloway as secretary of the Committee on Arrangements. The committee plans to present a program of operative clinics and demonstrations that will provide a comprehensive showing of their clinical activities in all departments of surgery at the Western Reserve University School of Medicine and the approved hospitals of Cleveland. Under the leadership of this committee, representative of the interests of all surgical specialties, a complete and varied program is assured for all who attend the Congress. The four-day program will include a presentation of the latest advances in diagnostic methods, surgical technique, operative procedures, pre- and postoperative care of the surgical patient. A preliminary clinical program is being prepared at the direction of the Committee on Arrangements and will appear in the October issue of this journal and the September *Bulletin* of the College. It is to be noted that clinics and demonstrations will be held in the hospitals on the afternoon of Tuesday, November 17, and the mornings and afternoons of succeeding days.

The clinical programs at the hospitals will be arranged to include a wide variety of subjects in general surgery, obstetrics and gynecology, fractures and other traumas, neurosurgery, thoracic surgery, orthopedic surgery, urology, ophthalmology and otorhinolaryngology. In the final program the presentations under these classifications will be so correlated that the visiting surgeon may devote his time to those clinics dealing with the special subjects in which he is most interested. During the Congress the complete detailed clinical program for each day will be posted in the form of bulletins at headquarters during the afternoon of the preceding day and distributed in printed form each morning.

### EXECUTIVE COMMITTEE

| | |
|---|---|
| Thomas E. Jones, Chairman | C. Lee Graber |
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### GENERAL ASSEMBLY

The opening session of the Congress, at 9:30 on Tuesday morning, will be a general assembly at headquarters for surgeons, hospital representa-

tives, and others. Dr. Irvin Abell, Chairman of the Board of Regents, will present a report on the field activities of the College, including the official announcement of the approved lists of hospitals, cancer clinics, hospitals approved for graduate training in surgery and the surgical specialties, medical services in industry, and medical motion pictures. Dr. W. Edward Gallie, of Toronto, President of the College, will speak on "Medical and Hospital Service in the War." The program for this session includes the following:

Major General James C. Magee, Surgeon General, United States Army, "Army Medical Service in the War."

Rear Admiral Ross T. McIntire, Surgeon General, United States Navy, "Naval Medical Service in the War."

Thomas Parran, M. D., Surgeon General, United States Public Health Service, "The Health of the Nation in Wartime."

Colonel George Baehr, Chief Medical Officer, Office of Civilian Defense, "Civilian Defense in its Relation to Medical and Hospital Service."

Frank H. Lahey, M.D., Chairman of Directing Board, Procurement and Assignment Service, "The Procurement and Assignment Service."

### PRESIDENTIAL MEETING AND CONVOCATION

At the Presidential Meeting and Convocation, on Tuesday evening at 8:15 in the Music Hall of the Cleveland Public Auditorium, the new officers of the College will be inaugurated, and the 1942 class of initiates received into fellowship. Distinguished surgeons from foreign countries attending the Congress will be introduced, following which the presidential address will be delivered by Dr. W. Edward Gallie, of Toronto. The new officers are:

Irvin Abell, M.D., Louisville, President.

Leland S. McKittrick, M.D., Boston, First Vice President.

F. Phinizy Calhoun, M.D., Atlanta, Second Vice President.

Participating in the program for this session are the following:

Major General James C. Magee, Surgeon General, United States Army.

Rear Admiral Ross T. McIntire, Surgeon General, United States Navy.

Thomas Parran, M. D., Surgeon General, United States Public Health Service.

Colonel George Baehr, Chief Medical Officer, Office of Civilian Defense.

### PANEL DISCUSSIONS ON WAR SURGERY

The value of the panel discussion as a medium of conveying information on selected subjects has been amply demonstrated at previous sessions of the Congress, sectional meetings, and the "War Sessions," that were held throughout the country during the early part of the present year. The Board of Regents has deemed it wise to use this medium as the principal method for the presentation of subjects at the 1942 Clinical Congress. Master panels have been planned for each afternoon, Tuesday through Friday, and on Wednesday, Thursday, and Friday evenings.

The restriction of the program to subjects dealing, for the most part, directly with war surgery has made it desirable to arrange these panel discussions so that they will be held consecutively rather than synchronously. This arrangement will enable surgeons attending the Congress to be present at each of the panel discussions, all of which will be held in the Cleveland Public Auditorium, which affords ample accommodations.

Surgeons who are in active military medical service will be among the speakers and collaborators in all of the panel discussions. Other eminent surgeons will also participate and questions from the floor will be welcomed. A few of the subjects and the leaders of discussions are as follows:

Shock, Blood and Blood Substitutes, Burns, and Combatting Chemical Warfare—Alfred Blalock, M. D., Baltimore.

Wounds in General—Allen O. Whipple, M.D., New York.

Wounds of the Chest—Evarts A. Graham, M.D., St. Louis.

War Injuries to the Skull—Howard C. Naffziger, M.D., San Francisco.

War Injuries to the Face—Robert H. Ivy, M.D., Philadelphia.

Anesthesia—Ralph T. Knight, M.D., Minneapolis.

Fractures—Lieutenant Colonel Robert H. Kennedy, M.C., U.S.A., Washington.

Transportation of the wounded and their treatment at the various types of hospitals and stations established by the military services, as well as aboard airplanes and ships, by the medical corps of the Army and Navy, will be the featured subject at another master panel.

On Wednesday evening, in addition to the panel discussions, the annual oration on surgery will be delivered by Captain Frederick R. Hook, M.C., U.S.N., Washington, on the subject of "Wounds in Combat." The following symposium will be presented on the same evening:

Preventive Aspects of Tropical Diseases, Captain Charles S. Stephenson, M.C., U.S.N., Washington.

Prevention of Acute Infectious Diseases, Colonel Hugh J. Morgan, M.C., U.S.A., Washington.

Venereal Disease, Lieutenant Colonel T. B. Turner, M.C., U.S.A., Washington.

Gynecology and Obstetrics in Their Relation to the War, J. Raglan Miller, M. D., Hartford, Conn.

### FORUMS ON FUNDAMENTAL SURGICAL PROBLEMS

The "Forums on Fundamental Surgical Problems," introduced with outstanding success at the 1941 Clinical Congress in Boston, will again have an important place on the program. Under the

chairmanship of Dr. Owen H. Wangensteen, of the University of Minnesota, a committee is formulating plans in detail. Through this forum, which will be held on Wednesday, Thursday and Friday mornings, an opportunity will be given the younger men, representing various university departments of surgery, to present the important results of their clinical and experimental research work before a large surgical meeting. Heretofore these younger men have seldom been able to present their original work and ideas, since many of them have not yet qualified for membership in the principal surgical societies.

Surgery today is concerned not only with anatomy and pathology, but to a growing extent with physiology, chemistry, and physics. Hence it is felt that the presentation of selected material of this type broadens the Clinical Congress program and is of great benefit to the surgeons attending the sessions.

No prepared discussions are planned but opportunity to ask questions will be afforded. Ten minutes is allotted to each presentation. Some of the best examples of new and highly constructive developments in surgery are expected to be presented in these Forums.

### SURGERY OF THE EYE, EAR, NOSE AND THROAT

Operative clinics and demonstrations in surgery of the eye, ear, nose and throat will be given daily at the hospitals. In addition, the general program of the Clinical Congress includes many features of special interest to those surgeons whose practice is limited to ophthalmology and otorhinolaryngology. Also planned for this group are a series of clinical conferences on Wednesday, Thursday, and Friday mornings at headquarters. In these conferences subjects of timely interest to specialists in these fields, will be discussed in small groups. Outstanding men will lead the discussions and opportunity will be provided for questions and participation.

Programs are being prepared for panel discussions on Wednesday, Thursday, and Friday evenings. Preceding each morning and evening session, selected motion picture films on subjects related to these special fields will be exhibited.

### HOSPITAL STANDARDIZATION CONFERENCE

The twenty-fifth annual Hospital Standardization Conference will open at 9:30 on Tuesday morning, in the Cleveland Public Auditorium, with a general assembly of surgeons, hospital representatives and others, the program for which appears on a preceding page. In his opening address, Dr. Irvin Abell, Chairman of the Board of Regents, will summarize the results of a quarter of a century of work in this department, and will officially announce the 1942 list of approved hospitals, hospitals approved for graduate training in surgery, and approved cancer clinics.

The subjects to be discussed at the Tuesday afternoon session have to do with adjusting hospital administration and services to present war conditions, maintaining essential man power in civilian hospitals, the needs of the armed forces for medical and nursing personnel, and include a special report on what has been accomplished in the Canadian hospitals in respect to these problems.

A series of panel discussions is planned which are to be centered around a general theme, with discussion of various aspects by well-known authorities. One panel will deal with the newer procedures in therapies developed during the war. Other panels will deal with shock, flesh wounds, burns, fractures, head and chest injuries, and their administrative or service significance. The problem of maintaining standards of service for medical staff conferences, pathological, x-ray, and anesthesia services will be discussed in another panel. Under the title of "Responsibility of the Administrative Staff in Dealing with Common Emergency Procedures," the subjects to be presented include post-tonsillectomy hemorrhage, respiratory obstruction, sudden collapse of postoperative patient due to pulmonary embolus, respiratory failure, acute cardiac attack (coronary thrombosis), sudden collapse on operating table, hemorrhage (acute and postpartum), and acute poisoning. The problem of maintaining adequate medical records in civilian hospitals will be the subject of another panel. Participating in these panels will be surgeons, surgical specialists, pathologists, anesthesiologists, and hospital administrators. The program will include especially arranged group conferences and demonstrations in selected hospitals, open forums and round-table conferences, and the showing of motion pictures of especial interest to hospital personnel. The aim is to provide features of interest to all types of hospital workers, administrators, department heads, personnel, members of the medical staffs, and governing boards.

Sustained interest in the College program of graduate training in surgery and the surgical specialties has been evidenced by the majority of hospitals suitable for such training. Opportunities will be provided for the discussion of individual problems. Many reports have been received showing that strenuous efforts are being made by most hospitals to preserve the essential features of their program despite the loss of men

for war service. Representatives of hospitals will be invited to discuss their plans for maintaining the College program, with a view to its adaptation to postwar needs. It is to be noted that the master panel on Friday afternoon, dealing with transportation of the wounded, mentioned on a previous page, will be a joint session for surgeons and hospital personnel, and will afford an excellent opportunity for hospital representatives to hear directly from the officers of the medical corps of the Army and the Navy concerning the various types of hospitals and stations that have been established both on land and on ships.

### CANCER CONFERENCE

A cancer conference, sponsored by the Cancer Committee of the College, will be held on Thursday morning. The subjects to be discussed will be those which are of immediate interest, indicating new lines of research, methods of attacking the cancer problem, and results obtained. Some methods of organization in cancer control will also be presented.

### SURGICAL MOTION PICTURES

Daily presentation at headquarters of a large and varied program of surgical motion pictures is planned. The latest available films, on a wide variety of subjects of interest to the surgeon, will be included. Both sound and silent, standard and color films, that have been approved by the Committee on Medical Motion Pictures will be shown.

### ADVANCE REGISTRATION AND REGISTRATION FEES

The hospitals and medical school of Cleveland afford accommodations for a large number of visiting surgeons, but attendance must be limited at the clinics to the number than can be comfortably accommodated. It is expected, therefore, that surgeons who wish to attend the Congress will register in advance. As in previous years, admission to clinics and demonstrations in the hospitals and to certain of the scientific meetings at headquarters will be controlled by means of tickets issued to the visiting surgeons on application at the registration desk. This plan provides for the distribution of visitors and helps to insure against overcrowding. Visiting surgeons are urged to cooperate in making the clinic ticket plan a success.

In accordance with a resolution adopted by the Board of Regents, fellows of the College whose dues are paid to December 31, 1941, initiates of the class of 1942, and fellows in military service will not be required to pay a registration fee for the 1942 Clinical Congress. For endorsed junior candidates the fee is $5.00. Surgeons, not fellows, who attend as invited guests of the College, will pay a registration fee of $10.00.

For purposes of identification at the registration desk, fellows should present their fellowship cards. Those surgeons who pay the registration fee in advance will receive a formal receipt which they will exchange for a general admission card upon presentation at the registration desk in the Cleveland Public Auditorium.

### HEADQUARTERS—TECHNICAL EXHIBITION

Headquarters for the Congress will be established at the Cleveland Public Auditorium, which affords unusual facilities for accommodating the Congress. All activities except the clinics at the hospitals will be held in this building.

The Technical Exhibition, together with the registration and clinic ticket desk, will be located in the arena on the main floor of the Auditorium. The daily clinical program, in the form of bulletins, will be posted there. Leading manufacturers of surgical instruments and supplies, sutures, dressings, pharmaceuticals, operating room equipment, x-ray apparatus and hospital equipment of all kinds, as well as publishers of medical books will be represented in the exhibition. An opportunity for careful inspection of the latest products of all those industries which are aiding the work of the surgeon and the hospital, will be provided for the visiting surgeons and hospital personnel.

### CLEVELAND HOTELS AND THEIR RATES

Cleveland has many first-class hotels, several within walking distance of the Public Auditorium, providing ample hotel facilities at reasonable rates. It is suggested that reservation of hotel accommodations be made at an early date. The following hotels are recommended by the Committee:

| | Minimum rate with bath | |
|---|---|---|
| | Single | Double |
| Allerton, Chester at East 13th St. | $2.50 | $4.00 |
| Auditorium, St. Clair at East 6th St. | 2.00 | 4.00 |
| Carter, Prospect at East 9th St. | 3.00 | 4.50 |
| Cleveland, Public Square | 3.00 | 4.50 |
| Hollenden, 610 Superior Ave., N.E. | 3.00 | 4.50 |
| Lake Shore, 12506 Edgewater Ave. | 3.50 | 6.00 |
| New Amsterdam, Euclid at East 22nd St. | 2.00 | 3.00 |
| Olmsted, Superior at East 9th St. | 2.50 | 4.00 |
| Sovereign, East Blvd. and East 105th St. | 3.00 | 4.00 |
| Statler, Euclid at East 12th St. | 3.00 | 4.50 |
| Tudor Arms, 10660 Carnegie Ave. | 3.30 | 5.00 |
| Wade Park Manor, Park Lane at East 107th St. | 3.50 | 5.00 |